121687

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Rosanne Kosson Examiner #: 80342 Date: 5/7/04
Art Unit: 1651 Phone Number 30 22923 Serial Number: 10/655,567
Mail Box and Bldg/Room Location: Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Anti-tumor agent

Inventors (please provide full names): Futoshi okada, Masuo Hosokawa, Hiroshi Shionoya

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please see attached page.

(SIIC) CLAIM

****

STAFF USE ONLY

Searcher: D. Schreiber
Searcher Phone #: 272-25-26
Searcher Location: Remsen E01 A61
Date Searcher Picked Up: 5/11
Date Completed: 5/13
Searcher Prep & Review Time: 14
Clerical Prep Time: _____
Online Time: 73

Type of Search

NA Sequence (#)	_____
AA Sequence (#)	_____
Structure (#)	_____
Bibliographic	V
Litigation	_____
Fulltext	_____
Patent Family	_____
Other	_____

Vendors and cost where applicable

STN	315.15
Dialog	_____
Questel/Orbit	_____
Dr.Link	_____
Lexis/Nexis	_____
Sequence Systems	_____
WWW/Internet	_____
Other (specify)	_____

EIC 1600/1700 (rev. 01)

STIC Search Report

Biotech-Chem Library

ref. delivery. -22550 -22520

STIC Database Tracking Number: 121687

TO: Rosanne Kosson
Location: REM-3B84&3E71
Art Unit: 1651
Thursday, May 13, 2004

Case Serial Number: 10/655567

From: David Schreiber
Location: Biotech-Chem Library
Remsen E01A61
Phone: 272-2526

david.schreiber@uspto.gov

Search Notes

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

Mary Hale, Information Branch Supervisor
Remsen Bldg. 01 D86
571-272-2507

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC-Biotech-Chem Library Remsen Bldg.

```
=> d his 1[redacted]

     (FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, WPIDS, SCISEARCH, AGRICOLA'
     ENTERED AT 09:18:07 ON 13 MAY 2004)
L33          58 DUP REM L32 (20 DUPLICATES REMOVED)

=> d que 133
L1         1237 SEA OKADA F?/AU
L2         3207 SEA HOSOKAWA M?/AU
L3          136 SEA SHIONOYA H?/AU
L4         4388 SEA (L1 OR L2 OR L3)
L5           50 SEA L4 AND (SOD# OR SUPEROXIDE?)
L6           28 SEA L5 AND (CANCER? OR TUMOR# OR TUMOUR# OR NEOPLAS? OR
                CARCINO? OR MALIGNAN?)
L7            1 SEA L6 AND GLIADIN#
L8       909228 SEA (TREAT? OR ADMINIST? OR THERAP?) (5A)(CANCER? OR TUMOR# OR
                TUMOUR# OR NEOPLAS? OR CARCINO? OR MALIGNAN?)
L10      168183 SEA SOD OR SODS OR SUPEROXIDE(3A) DISMUTASE#
L11        1793 SEA L8 AND L10
L12           2 SEA L11 AND GLIADIN#
L13           5 SEA L8 AND GLIADIN#
L15           8 SEA (CANCER? OR TUMOR# OR TUMOUR# OR NEOPLAS? OR CARCINO? OR
                MALIGNAN?) (5A) GLIADIN#
L16          14 SEA MELON (5A) L10
L17           5 SEA (CANCER? OR TUMOR# OR TUMOUR# OR NEOPLAS? OR CARCINO? OR
                MALIGNAN?) AND L16
L18        1997 SEA (COAT? OR STABILIZ? OR STABILIS? OR MODIF?)(5A) L10
L19         147 SEA L18 (5A)(PROTEIN? OR PEPTIDE# OR LIPID?)
L20          10 SEA (CANCER? OR TUMOR# OR TUMOUR# OR NEOPLAS? OR CARCINO? OR
                MALIGNAN?) AND L19
L21         112 SEA (CANCER? OR TUMOR# OR TUMOUR# OR NEOPLAS? OR CARCINO? OR
                MALIGNAN?) AND L18
L22           3 SEA L21 AND LECITHIN#
L23           9 SEA L21 AND LIPID?
L24           6 SEA L21 AND FAT?
L25          39 SEA L7 OR L12 OR L13 OR L15 OR L17 OR L20 OR (L22 OR L23 OR
                L24)
L30         971 SEA L10(3A) CONJUGA?
L31          41 SEA (CANCER? OR TUMOR# OR TUMOUR# OR NEOPLAS? OR CARCINO? OR
                MALIGNAN?) AND L30
L32          78 SEA L25 OR L31
L33          58 DUP REM L32 (20 DUPLICATES REMOVED)


=> d ibib abs 133 1-58

L33  ANSWER 1 OF 58  HCAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:271480  HCAPLUS
DOCUMENT NUMBER:          140:281374
TITLE:                    Antitumor agents containing coated SOD
INVENTOR(S):              Okada, Futoshi; Hosokawa, Masuo;
                          Shionoya, Hiroshi
PATENT ASSIGNEE(S):       Asama Chemical Co., Ltd., Japan; Konbi K. K.; Izoseru
                          SA
SOURCE:                   Jpn. Kokai Tokkyo Koho, 8 pp.
                          CODEN: JKXXAF
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
```

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004099459	A2	20040402	JP 2002-259766	20020905

PRIORITY APPLN. INFO.: JP 2002-259766 20020905

AB Title agents are claimed. Thus, oral administration of 10 mg/kg Oxykine (**gliadin**-coated **melon SOD**) to **tumor** bearing mice significantly prevented **tumor** growth.

L33 ANSWER 2 OF 58 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004193800 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15094390
TITLE: A novel anti-oxidant and anti-**cancer** strategy: a peptoid anti-inflammatory drug **conjugate** with **SOD** mimic activity.
AUTHOR: Bailey Mark A; Ingram Matthew J; Naughton Declan P
CORPORATE SOURCE: School of Pharmacy and Biomolecular Sciences, University of Brighton, Cockcroft Building, Moulsecoomb, Brighton BN2 4GJ, UK.
SOURCE: Biochemical and biophysical research communications, (2004 May 14) 317 (4) 1155-8.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040420
Last Updated on STN: 20040420

AB Activation of reactive oxygen and nitrogen species (RONS) by redox-active metal ions has been proposed to contribute to oxidative damage in inflamed tissues. Here, we report a dual-function anti-oxidant conjugate comprising an anti-inflammatory agent (5-aminosalicylic acid) and a chelator with potential as a superoxide dismutase mimic. The conjugate ethylenediaminetetraacetic acid bis-(5-aminosalicylic acid methyl ester) [EBAME] chelates Cu(II) ions in a 1:1 ratio, as assessed spectrophotometrically using Job's method. Superoxide dismutase (SOD) activity was determined for the Mn(II)-conjugate as 0.758+/-0.130U at a concentration of 0.99microM. In inflamed tissues, peptidase mediated release of active 5-ASA would also release the EDTA chelator which has significant SOD mimic activity when complexed to Cu(II) ions. Thus, EBAME has potential as a dual-function anti-inflammatory agent with reduced gastric irritability.

L33 ANSWER 3 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2004:261058 SCISEARCH
THE GENUINE ARTICLE: 801UD
TITLE: Poly(vinylpyrrolidone-co-dimethyl maleic acid) as a novel renal targeting carrier
AUTHOR: Yamamoto Y; Tsutsumi Y (Reprint); Yoshioka Y; Kamada H; Sato-Kamada K; Okamoto T; Mukai Y; Shibata H; Nakagawa S; Mayumi T
CORPORATE SOURCE: Osaka Univ, Grad Sch Pharmaceut Sci, Dept Biopharmaceut, 1-6 Yamadaoka, Suita, Osaka 5650871, Japan (Reprint); Osaka Univ, Grad Sch Pharmaceut Sci, Dept Biopharmaceut, Suita, Osaka 5650871, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: JOURNAL OF CONTROLLED RELEASE, (5 MAR 2004) Vol. 95, No. 2, pp. 229-237.

Search completed by David Schreiber x22526

Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0168-3659.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 28

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Poly(vinylpyrrolidone-co-dimethyl maleic acid) (PVD) was found to have high renal-targeting capability and safety as a drug carrier. To optimize the renal drug delivery system using PVD, the relationship between the molecular weight of PVD and its renal accumulation were evaluated in mice by their intravenous injection. It was found that the molecular size of 6-8 kDa was associated with the highest renal accumulation. The specific bioactivity of PVD-**conjugated superoxide dismutase** (**SOD**) relative to that of unmodified SOD gradually decreased with an increase in the degree of modification to **SOD** with PVD6K. The **conjugated SOD** (L-PVD-**SOD**) with the molecular size of 73 kDa, which had comparable specific bioactivity with native SOD, showed longer plasma half-life than native SOD. About sixfold more L-PVD-SOD was distributed to the kidneys than native SOD 3 h after intravenous injection, whereas extensive PVD modification did not enhance the renal accumulation of SOD. This L-PVD-SOD effectively accelerated recovery from mercuric chloride-induced acute renal failure in vivo. These results suggest that L-PVD-SOD may be the optimal derivative as a potential therapeutic agent to various renal diseases. (C) 2004 Elsevier B.V. All rights reserved.

L33 ANSWER 4 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:719332 HCAPLUS
DOCUMENT NUMBER: 139:219381
TITLE: Coupling proteins to a modified polysaccharide, especially oxidized hydroxyethyl starch for use as drugs
INVENTOR(S): Hemberger, Juergen; Orlando, Michele
PATENT ASSIGNEE(S): Biotechnologie - Gesellschaft Mittelhessen MbH, Germany
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074087	A1	20030912	WO 2003-EP2083	20030228
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10209821	A1	20030925	DE 2002-10209821	20020306

PRIORITY APPLN. INFO.: DE 2002-10209821 A 20020306

Search completed by David Schreiber x22526

AB The invention relates to a method for coupling proteins to a starch-derived modified polysaccharide. The binding interaction between the modified polysaccharide and the protein is based on a covalent bond which is the result of a coupling reaction between the terminal aldehyde group or a functional group of the modified polysaccharide mol. resulting from the chemical reaction of this aldehyde group and a functional group of the protein which reacts with the aldehyde group or with the resulting functional group of the polysaccharide mol. The bond directly resulting from the coupling reaction can be optionally modified by a further reaction to the aforementioned covalent bond. The invention further relates to pharmaceutical compns. that comprise conjugates formed in this coupling process and to the use of said conjugates and compns. for the prophylaxis or therapy of the human or animal body. Thus high (130 kD) and low mol. weight (10 kD) hydroxyethyl starch was selectively oxidized and coupled to various proteins, e.g. human serum albumin, myoglobin, superoxide dismutase, streptokinase, asparaginase.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 5 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:697052 HCAPLUS
DOCUMENT NUMBER: 139:209957
TITLE: Modified human manganese superoxide dismutase and therapeutic use
INVENTOR(S): Mancini, Aldo
PATENT ASSIGNEE(S): Istituto Nazionale per lo Studio e la Cura dei Tumori Fondazione GiovanniPascale, Italy
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072768	A2	20030904	WO 2003-EP2017	20030227
WO 2003072768	A3	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2002-MI404 A 20020228
AB The present invention refers to a novel modified form of hMnSOD that can be produced and secreted from cells of human liposarcoma in continuous culture. This protein is obtainable :by ionic exchange chromatog., gel filtration and immunoaffinity techniques from the culture medium in which these cells release it. Moreover the present invention refers to the use of this modified hMnS.OD for preparation of a medicament for prevention and therapy of **tumors**, of septic and traumatic shock, diabetic neuropathy, post-herpetic neuritis and **malignant** hyperthermia and for healing of cutaneous lesions.

Search completed by David Schreiber x22526

L33 ANSWER 6 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:508484 HCAPLUS
DOCUMENT NUMBER: 139:57985
TITLE: Immunostimulative compositions containing β-glucan-containing products and **superoxide dismutase** with fats and proteins
INVENTOR(S): Abe, Kuniaki; Suga, Tatsuhiko; Takekawa, Wakoto
PATENT ASSIGNEE(S): Wellness Movement K. K., Japan; Konbi K. K.; Kyowa Engineering Co., Ltd.; Sundry Co., Ltd.; Izoseru SR
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003183176	A2	20030703	JP 2002-281360	20020926

PRIORITY APPLN. INFO.: JP 2001-311336 A 20011009
AB The invention relates to an immunostimulative composition suitable for use in a food for prevention or treatment of immune disease, wherein the composition is characterized by containing (1) β-glucan-containing mushroom products, i.e. Agaricus and/or Phellinus linteus, and (2) a composition containing **superoxide dismutase** (**SOD**), fat, and protein. A mixture containing a wheat **gliadin**-including **melon**-derived **SOD** composition (Oxykaine) and Agaricus blazei extract was formulated and orally **administered** to a **tumor**-bearing mouse to examine the immunostimulative effect.

L33 ANSWER 7 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:107165 HCAPLUS
DOCUMENT NUMBER: 136:172754
TITLE: Highly reactive branched polymer and proteins or peptides conjugated with the polymer
INVENTOR(S): Park, Myung-Ok; Lee, Kang-Choon; Cho, Sung-hHe
PATENT ASSIGNEE(S): S. Korea
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009766	A1	20020207	WO 2001-KR1209	20010713

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: KR 2000-44046 A 20000729

Search completed by David Schreiber x22526

AB The present invention relates to new biocompatible polymer derivs., and a protein-polymer or a peptide-polymer which is produced by conjugation of biol. active protein and peptide with the biocompatible polymer derivs. More particularly, the present invention relates to a highly reactive branched biocompatible polymer derivative containing a long linker between polymer derivs. and protein or peptide mols., which is minimized in decrease the biol. activity of proteins by conjugating the less number of polymer derivs. to the active sites of proteins, improved in water solubility, and protected from being degraded by protease. In hence, the highly reactive branched biocompatible polymer-proteins or peptides conjugates with long linker retain the biol. activity for a long period of time and improve a bioavailability of bioactive proteins and peptides. For example, activated PEG-interferon conjugates were prepared by adding 3 mg of succinic N-hydroxysuccinimidyl di-PEG to 3 mg of interferon in 0.1 M phosphate buffer solution, pH 7.0 at ambient temperature The reaction was stopped with 0.1 M glycine and the excess reagents were using Centricon-30.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 8 OF 58 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-735014 [80] WPIDS
DOC. NO. CPI: C2002-208137
TITLE: New superoxide dismutase compositions, used for e.g. prevention and treatment allergies, inflammatory disorders, and degenerative disorders, comprise Cucumis melo extract and a liposoluble **fatty** material.
DERWENT CLASS: B05 C03 D13 D21
INVENTOR(S): DREYER, A; GINOUX, J P; LACAN, D; ROCH, P; YARD, C; GINOUX, J
PATENT ASSIGNEE(S): (BIOO-N) BIO-OBTENTION SC; (DREY-I) DREYER A; (GINO-I) GINOUX J; (LACA-I) LACAN D; (ROCH-I) ROCH P; (YARD-I) YARD C
COUNTRY COUNT: 3
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2822381	A1	20020927	(200280)*		39
US 2002182269	A1	20021205	(200301)		
JP 2003002840	A	20030108	(200315)		54
US 2003203052	A1	20031030	(200372)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
FR 2822381	A1	FR 2001-3750	20010320
US 2002182269	A1	US 2001-850037	20010508
JP 2003002840	A	JP 2002-79019	20020320
US 2003203052	A1 Div ex	US 2001-850037	20010508
		US 2003-446672	20030529

PRIORITY APPLN. INFO: FR 2001-3750 20010320
AN 2002-735014 [80] WPIDS
AB FR 2822381 A UPAB: 20021212
NOVELTY - Compositions (I) comprising a vegetable extract rich in

superoxide dismutase coated or microencapsulated with a liposoluble **fatty** material, are new.

DETAILED DESCRIPTION - Compositions (I) comprising a vegetable extract rich in superoxide dismutase which is a proteic extract of Cucumis melo, especially in powder form, coated or microencapsulated with a liposoluble **fatty** material, are new.

ACTIVITY - Antiallergic; Dermatological; Antiinflammatory; Immunosuppressive; Antipsoriatic; Antiasthmatic; Antianemic; Cytostatic; Antiinfertility; Nootropic; Neuroprotective; Antiparkinsonian; Anti-HIV; Hepatotropic; Virucide.

MECHANISM OF ACTION - Superoxide dismutase liberator.

USE - (I) are used for the prevention and treatment of allergies, inflammatory disorders, and degenerative disorders. In particular for the prevention and treatment of eczema, vitiligo, psoriasis, lupus, cutaneous fibroses, to protect against UV radiation, to improve graft cicatrization, asthma, anemia, male sterility, anthopathias, degenerative disorders such as Crohn's disease, Parkinson's disease, Alzheimer's disease, colorectal **cancers**, various fibroses, degeneration due to AIDS or hepatitis C, and degeneration due to administration of a medicament (claimed).

ADVANTAGE - The formulations avoid the use of animal material as source of superoxide dismutase.

Dwg.0/8

L33 ANSWER 9 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:144542 HCAPLUS
DOCUMENT NUMBER:	138:368048
TITLE:	Effect of conjugated linoleic acid on colon **tumor** incidence and antioxidant enzymes and fecal excretion of secondary bile acids in DMH-treated rats
AUTHOR(S):	Kim, Kyung-Hee; Kang, Keum-Jee; Park, Hyun-Suh
CORPORATE SOURCE:	Chonnam University Research Institute of Medical Sciences, Gwangju, 501-746, S. Korea
SOURCE:	Hanguk Yongyang Hakhoechi (2002), 35(10), 1038-1044 CODEN: HYHJA3; ISSN: 0367-6463
PUBLISHER:	Korean Nutrition Society
DOCUMENT TYPE:	Journal
LANGUAGE:	Korean

AB The study was designed to observe the effect of conjugated linoleic acid (CLA) on **tumor** incidence, eicosanoid formation and antioxidant enzyme activities in colonic mucosa and the fecal excretion of deoxycholic acid and lithocholic acid in 1,2-dimethylhydrazine (DMH)-treated rats. One hundred twenty male Sprague Dawley rats were divided into 2 groups, BT (beef tallow diet) group and FO (fish oil diet) group, and each group was again subdivided into 2 groups depending on CLA supplementation, i.e. 4 groups of BT, BTC, FO, FOC. All rats were fed an exptl. diet for 30 wk, which contained 12% (wt/wt) total dietary fat including 1% (wt/wt) CLA, and were i.m. injected with DMH for 6 wk to give total dose of 180 mg/kg body. CLA-supplemented to the BT and FO diet reduced **tumor** incidence, eicosanoid (PGE2 and TXA2) level in colonic mucosa. N-3 fatty acids (mainly DHA) of the fish oil diet (FO, FOC group) also reduced **tumor** incidence and significantly reduced eicosanoid (PGE2 and TXA2) level in colonic mucosa. CLA supplementation and n-3 fatty acid significantly increased colonic mucosal level of superoxide dismutase and glutathione peroxidase activities but reduced secondary bile acid (deoxycholic acid and lithocholic acid) excretion in the feces. In conclusion, CLA supplementation and n-3 fatty acid could reduce **tumor** incidence by reducing eicosanoids and increasing antioxidant enzyme activities in colon and decreasing the excretion of deoxycholic

acid and lithocholic acid in the feces. The data might suggest that CLA supplementation and DHA rich fish oil may modulate colon **carcinogenesis.**

L33 ANSWER 10 OF 58 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002389920 EMBASE
TITLE: Immunomodulating activities of soluble synthetic polymer-bound drugs.
AUTHOR: Rihova B.
CORPORATE SOURCE: B. Rihova, Institute of Microbiology, ASCR, Videnska 1083, 14220 Prague 4, Czech Republic. rihova@biomed.cas.cz
SOURCE: Advanced Drug Delivery Reviews, (13 Sep 2002) 54/5 (653-674).
Refs: 135
ISSN: 0169-409X CODEN: ADDREP
PUBLISHER IDENT.: S 0169-409X(02)00043-1
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The introduction of a synthetic material into the body always affects different body systems, including the defense system. Synthetic polymers are usually thymus-independent antigens with only a limited ability to elicit antibody formation or to induce a cellular immune response against them. However, there are many other ways that they influence or can be used to influence the immune system of the host. Low-immunogenic water-soluble synthetic polymers sometimes exhibit significant immunomodulating activity, mainly concerning the activation/suppression of NK cells, LAK cells and macrophages. Some of them, such as poly(ethylene glycol) and poly[N-(2-hydroxypropyl)methacrylamide], can be used as effective protein carriers, as they are able to reduce the immunogenicity of conjugated proteins and/or to reduce non-specific uptake of liposome/nanoparticle-entrapped drugs and other therapeutic agents. Recently, the development of vaccine delivery systems prepared from biodegradable and biocompatible water-soluble synthetic polymers, microspheres, liposomes and/or nanoparticles has received considerable attention, as they can be tailored to meet the specific physical, chemical, and immunogenic requirements of a particular antigen and some of them can also act as adjuvants.

L33 ANSWER 11 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:295746 HCAPLUS
DOCUMENT NUMBER: 136:384631
TITLE: Activation of macrophages by gliadin fragments: isolation and characterization of active peptide
AUTHOR(S): Tuckova, Ludmila; Novotna, Jana; Novak, Petr; Flegelova, Zuzana; Kveton, Tomas; Jelinkova, Lenka; Zidek, Zdenek; Man, Petr; Tlaskalova-Hogenova, Helena
CORPORATE SOURCE: Institute of Microbiology, Academy of Sciences of the Czech Republic, Prague, 14220/4, Czech Rep.
SOURCE: Journal of Leukocyte Biology (2002), 71(4), 625-631
CODEN: JLBIE7; ISSN: 0741-5400

Search completed by David Schreiber x22526

PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Celiac disease, induced by dietary gluten, is characterized by mucosal atrophy and local inflammation associated with cell infiltration and activation. Unlike other food proteins, gluten and its proteolytic fragments, besides inducing a specific immune response, were shown to activate components of innate immunity and cause, e.g., direct stimulation of TNF-α and IL-10 and a significant rise in NO production by peritoneal macrophages. The identity of the active fragments was established by separating the peptic digest of gliadin by RP-HPLC chromatog. The purest fraction with the highest activity was analyzed by mass spectrometry, and the gliadin peptide sequence was identified as VSFQQPQQQYPSSQ. This peptide (T) and its N- and C-terminally shortened forms (A, B, C and D, E, F) were synthesized. Peptide B (FQQPQQQYPSSQ) elicited the highest TNF-α, IL-10, and RANTES secretion and increase in IFN-γ-primed NO production by mouse macrophages. In contrast, C-terminally shortened peptides had a lower ability to stimulate macrophages than the native form.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 12 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:840197 HCAPLUS
DOCUMENT NUMBER: 138:72557
TITLE: Influence of conjugated vs. conventional linoleic acid on liver metastasis and hepatic lipid peroxidation in BOP-induced pancreatic **cancer** in Syrian hamster
AUTHOR(S): Kilian, M.; Mautsch, I.; Gregor, J. I.; Stahlknecht, P.; Jacobi, C. A.; Schimke, I.; Guski, H.; Wenger, F. A.
CORPORATE SOURCE: Department of General, Visceral, Vascular and Thoracic Surgery, Humboldt-University of Berlin, Berlin, 10117, Germany
SOURCE: Prostaglandins, Leukotrienes and Essential Fatty Acids (2002), 67(4), 223-228
CODEN: PLEAEU; ISSN: 0952-3278
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB While conjugated linoleic acid (CLA) is an essential fatty acid with anticarcinogenic effects, conventional linoleic acid (LA, C18:2n-6) can promote **tumor** growth in various exptl. studies probably due to high sensitivity to non-enzymic lipid peroxidn. To evaluate the impact of dietary LA and CLA (isomer mixture) on liver metastasis and lipid peroxidn. (LPO), 60 Syrian hamsters were injected weekly with 10 mg N-nitrosobis-2-oxopropylamine (BOP)/kg body weight s.c. for 12 wk and fed diets containing LA or CLA. The experiment was terminated after 24 wk. The incidence, number, and size of liver metastases were histol. determined The activities of antioxidant enzymes and concns. of hepatic lipid peroxidn. products were measured intra- and extrametastatically. The incidence, number, and size of liver metastases did not differ between the **tumor** groups. The antioxidant activity of glutathione peroxidase was higher in the non-metastatic liver, while the superoxide dismutase activity and lipid peroxidn. were increased in liver metastases. There was no difference between the groups fed LA and CLA in the impact on liver metastasis in rats with ductal pancreatic **cancer**.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 13 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:747647 HCAPLUS
DOCUMENT NUMBER: 135:308875
TITLE: Drugs retained in target tissue over long time
INVENTOR(S): Sato, Haruya; Hayashi, Eiko; Shirae, Hideyuki
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074399	A1	20011011	WO 2001-JP2604	20010328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001044602	A5	20011015	AU 2001-44602	20010328
EP 1279405	A1	20030129	EP 2001-917574	20010328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003103934	A1	20030605	US 2002-259773	20020930

PRIORITY APPLN. INFO.: JP 2000-93775 A 20000330
WO 2001-JP2604 W 20010328

AB Disclosed are a ligand attached to a polyethylene glycol wherein a polyethylene glycol chain is attached to a ligand having a binding affinity to a specific receptor or a protein (antigen, etc.) located on the cell membrane of a target tissue and being capable of avoiding the incorporation into cells; and medicines wherein a drug (a physiol. active substance, etc.) is attached to this polyethylene glycol chain. Thus, a novel ligand, which can be accumulated at a high concentration around a target tissue and has good retention properties in the blood, and excellent medicines, wherein a drug (a physiol. active substance, etc.) efficacious in the above target tissue is attached thereto, can be provided. (Gal)3-polyethylene glycol-interferon-α conjugate was prepared and administered to mice; higher concns. of interferons were determined in the plasma and liver tissues, as compared to the ones obtained by administration of unmodified interferons.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 14 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:18926 HCAPLUS
DOCUMENT NUMBER: 134:66178
TITLE: **Lecithin-modified superoxide dismutase** as an antifibrotic agent
INVENTOR(S): Takeuchi, Jun; Igarashi, Toshisato

PATENT ASSIGNEE(S): LTT Inst. Co., Ltd., Japan; Asahi Glass Co., Ltd.; Seikagaku Kogyo Co., Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001002585	A2	20010109	JP 1999-175381	19990622

PRIORITY APPLN. INFO.: JP 1999-175381 19990622

AB The anti- tissue conversion agent which contains the PC-SOD is offered. **Lecithin-modified superoxide dismutase** (**SOD**' (Q-B)m; SOD' = residue of superoxide dismutase; Q = chemical crosslinkage; B = hydrogen atom of hydroxyl group of lysolecithin at C2 of glycerol, m = >1 of lysolecithin for binding 1 mol. superoxide dismutase) is claimed as an antifibrotic agent and can be combined with antiinflammatory steroids, including prednisolone derivs., for treatment of fibrotic diseases (e.g. pulmonary fibrosis) and **cancer**.

L33 ANSWER 15 OF 58 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001477100 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11520596
TITLE: Targeting superoxide dismutase to renal proximal tubule cells inhibits nephrotoxicity of cisplatin and increases the survival of **cancer**-bearing mice.
AUTHOR: Nishikawa M; Nagatomi H; Nishijima M; Ohira G; Chang B J; Sato E; Inoue M
CORPORATE SOURCE: Department of Biochemistry, Osaka City University Medical School, 1-4-3 Asahimachi, Abeno-ku, Osaka, Japan.. nishikawa@med.osaka-cu.ac.jp
SOURCE: Cancer letters, (2001 Oct 10) 171 (2) 133-8.
Journal code: 7600053. ISSN: 0304-3835.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20011001
Entered Medline: 20010927

AB Because cis-diamminedichloroplatinum(II) (cisplatin) which generates reactive oxygen species induces renal dysfunction, administration of a large dose for killing **cancer** cells is highly limited. We recently synthesized a cationic **superoxide dismutase** (**SOD**) (hexamethylenediamine-**conjugated SOD**, AH-**SOD**) which rapidly accumulates in renal proximal tubule cells and inhibits oxidative injury of the kidney. Treatment of Ehrlich ascites **tumor** cells (EATC)-bearing mice with cisplatin sufficient for killing **tumor** cells increased their motality. The motality of cisplatin-treated EATC-bearing mice was markedly decreased by AH-SOD. These results suggest that targeting SOD to renal proximal tubule cells might permit the administration of high doses of cisplatin and related anticancer agents without causing renal injury.

L33 ANSWER 16 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:386273 HCAPLUS

DOCUMENT NUMBER: 136:156239
TITLE: Novel anticancer strategy by means of DIVEMA (copolymer of divinyl ether and maleic anhydride)
AUTHOR(S): Kondo, Tadashi; Hirano, Takashi; Todoroki, Ken; Ohashi, Shinichi
CORPORATE SOURCE: Department of Surgery, University of Tsukuba, Japan
SOURCE: Drug Delivery System (2001), 16(2), 106-113
CODEN: DDSYEI; ISSN: 0913-5006
PUBLISHER: Nippon DDS Gakkai Jimukyoku
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review. Development of anticancer drugs provides the significant achievement in the clin. treatment. However most of the clin. antitumor drugs have severe side effects such as leukocytepenta. To reduce side effects and enhance antitumor activity, the delivery of antitumor reagent should be controlled. One of the most effective methods to control the pharmacokinetics is the conjugation of antitumor drugs with polymeric carriers. We have developed novel conjugates of DIVEMA (copolymer of divinyl ether and maleic anhydride) with anticancer drugs (adriamycin and methotrexate) and cytokine (TNF-α). The conjugates proved to have more effective than anticancer drugs against murine **cancer** models including solid **tumors** with less toxicity. Such polymeric conjugates proved to be effective to improve the body distribution of bioactive proteins, which are quickly hydrolyzed by proteolytic enzymes in vivo. As a model of protein, we have examined the anti-inflammatory activity of the **conjugated** of **SOD** (**superoxide dismutase**) with DIVEMA. Liver resection and liver transplantation needs the effective protection of ischemia-reperfusion injury, which leads to organ failure. Some attempts have been made for protect ischemia-reperfusion injury by means of SOD. Due to the short half-life in vivo of SOD alone (less than 5 min), the clin. effectiveness of SOD was quite limited. Through dynamic observation of the liver microcirculation using intra-vital microscopy techniques, we have evaluated the effect of DIVEMA-SOD on ischemia-reperfusion liver injury. DIVEMA-SOD showed protective effect of ischemia-reperfusion injury significantly as compared to SOD alone. The copolymer of DIVEMA provides the possibility for great achievement of with cytokines, and organ protection in the transplantation medicine.

L33 ANSWER 17 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:293179 HCAPLUS
DOCUMENT NUMBER: 135:42082
TITLE: Benzo(a)pyrene-coated onto Fe2O3 particles-induced lung tissue injury: role of free radicals
AUTHOR(S): Garcon, G.; Garry, S.; Gosset, P.; Zerimech, F.; Martin, A.; Hannothiaux, M.-H.; Shirali, P.
CORPORATE SOURCE: Faculte de Medecine-Pole Recherche, GIP-CERESTE, Laboratoire Universitaire de Medecine du Travail et des Risques Professionnels, Lille, 59045, Fr.
SOURCE: Cancer Letters (Shannon, Ireland) (2001), 167(1), 7-15
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Lipid** peroxidn. (as malondialdehyde; MDA), activities of some antioxidant enzymes (as superoxide dismutase; SOD, glutathione peroxidase; GPx, glutathione reductase; GR), glutathione status, and oxidative DNA damage (as 8-hydroxy-2'-deoxyguanosine; 8-OHdG) were investigated in the lungs of rats exposed to hematite (Fe2O3; 3 mg), benzo(a)pyrene (B(a)P; 3

mg), or B(a)P (3 mg)-coated onto Fe2O3 particles (3 mg). Approx. 2-fold increases in MDA production were seen in animals exposed to Fe2O3, B(a)P, or B(a)P-coated onto Fe2O3 particles (P<0.01). Decreases in SOD activities were observed in rats treated with Fe2O3 (1.66-fold, P<0.01), B(a)P (1.66-fold, P<0.001) or B(a)P-coated onto Fe2O3 particles (1.43-fold, P<0.01). GPx and GR activities could not be detected. No alteration of the glutathione status was observed Significant increases in the 8-OHdG formation occurred in response to exposure to B(a)P (2.0-fold, P<0.01) or B(a)P-coated onto Fe2O3 particles (23.7-fold, P<0.001). Our results demonstrate also that Fe2O3 generates free radical-induced lung injury and is not an inert carrier. We established that exposure to B(a)P or B(a)P-coated onto Fe2O3 particles resulted in **lipid** peroxidn. and SOD inactivation, thereby leading to oxidative damages in DNA. The main findings of this work was that B(a)P-coated onto Fe2O3 particles caused higher lung concns. of 8-OHdG than B(a)P by itself. Hence, our data may explain why exposure to B(a)P-coated onto Fe2O3 particles resulted in a decreased latency and an increased incidence of lung **tumors** in rodents compared to exposure to B(a)P.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 18 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:911065 HCAPLUS
DOCUMENT NUMBER: 134:76386
TITLE: Amphiphilic drug-oligomer conjugates with hydrolyzable lipophile components and methods for making and using the same
INVENTOR(S): Ekwuribe, Nnochiri; Ramaswamy, Muthukumar; Rajagopalan, Jayanthi
PATENT ASSIGNEE(S): Protein Delivery, Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078302	A1	20001228	WO 2000-US16879	20000619
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6309633	B1	20011030	US 1999-336548	19990619
BR 2000011772	A	20020402	BR 2000-11772	20000619
EP 1196157	A1	20020417	EP 2000-942956	20000619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003502364	T2	20030121	JP 2001-504366	20000619
ZA 2001010099	A	20030307	ZA 2001-10099	20011207
NO 2001006143	A	20020218	NO 2001-6143	20011217

PRIORITY APPLN. INFO.: US 1999-336548 A 19990619
WO 2000-US16879 W 20000619

AB The present invention relates generally to hydrolyzable drug-oligomer conjugates, pharmaceutical compns. comprising such conjugates, and to methods for making and using such conjugates and pharmaceutical compns. For example, a conjugate of insulin, PEG, and oleic acid was prepared and can be orally administered.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 19 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:885433 HCAPLUS
DOCUMENT NUMBER: 134:280075
TITLE: Milk fat conjugated linoleic acid (CLA) inhibits growth of human mammary MCF-7 **cancer** cells
AUTHOR(S): O'Shea, Marianne; Devery, Rosaleen; Lawless, Fergal; Murphy, John; Stanton, Catherine
CORPORATE SOURCE: Teagasc, Dairy Products Research Centre, Fermoy, Ire.
SOURCE: Anticancer Research (2000), 20(5B), 3591-3601
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The relationship between growth and the antioxidant enzyme defense system in human MCF-7 (breast) **cancer** cells treated with bovine milk fat enriched with conjugated linoleic acid (CLA) was studied. Milk enriched in CLA was obtained from cows on pasture supplemented with full fat rapeseeds and full fat soybeans. Cell number decreased up to 90% ($p < 0.05$) and lipid peroxidn. increased 15- fold ($p < 0.05$) following incubation of MCF-7 cells for 8 days with increasing levels of milk fat yielding CLA concns. between 16.9 and 22.6 ppm. Growth suppression and prooxidant effects of milk fat CLA were independent of the variable composition of the milk fat samples, suggesting that CLA was the active ingredient in milk fat responsible for the cytotoxic effect. Mixts. containing isomers of CLA (c9, t11-, t10, c12-, c11, c13- and minor amts. of other isomers) and linoleic acid (LA) at similar concns. to the milk fat samples were as effective at inhibiting growth and stimulating peroxidn. of MCF-7 cells as the milk fatty acids. Incubation of the cells with the c9, t11 CLA isomer (20 ppm) or the mixture of CLA isomers (20 ppm) for 8 days resulted in a 60% decrease ($p < 0.05$) in viability compared with untreated controls and was significantly ($p < 0.05$) more effective than incubation with the t10, c12 CLA isomer (20 ppm), which caused only a 15% decrease in cell nos. under similar conditions. A 25% increase ($p < 0.05$) in cell proliferation occurred when LA (20 ppm) alone was incubated with MCF-7 cells for 8 days. 14C-CLA was preferentially incorporated into the phospholipid fraction of the MCF-7 cell lipids in a dose-dependent manner and CLA accumulated in cell membranes more efficiently when the cells were incubated in the presence of milk fat than the c9, t11 synthetic CLA isomer. Superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx) activities were induced in MCF-7 cells exposed to milk fat (containing 16.9-22.6 ppm CLA) over 8 days. The data indicate that milk fat triglyceride-bound CLA, consisting primarily of the c9, t11 isomer, was cytotoxic towards MCF-7 cells.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 20 OF 58 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:99440 BIOSIS
DOCUMENT NUMBER: PREV200100099440
TITLE: Polysaccharide Krestin enhances manganese superoxide dismutase activity and mRNA expression in mouse peritoneal

macrophages.

AUTHOR(S): Pang, Zhan-Jun [Reprint author]; Chen, Yuan; Zhou, Mei
CORPORATE SOURCE: Research Laboratory of Free Radical Medicine, First Military Medical University, Guangzhou, 510515, China
SOURCE: American Journal of Chinese Medicine, (2000) Vol. 28, No. 3-4, pp. 331-341. print.
CODEN: AJCMBA. ISSN: 0192-415X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Feb 2001
Last Updated on STN: 15 Feb 2002

AB Manganese superoxide dismutase (MnSOD), an inductive antioxidant enzyme, can protect cells from oxidative injury to the mitochondria. The elevation of MnSOD activity in cells can effectively prevent many diseases associated with oxidative stress. Polysaccharide Krestin (PSK), a kind of protein-bound polysaccharide extracted from Coriolus versicolor, is used as an immune response modifier in anti-**tumor** therapy. We have previously found that PSK could alleviate the oxidative injury that oxidized low density lipoprotein (Ox-LDL) brought to monocytes/macrophages, and therefore had some preventive or therapeutic effect on atherosclerosis. In order to find out if the effects of PSK were associated with the alteration of antioxidant enzymes, we investigated its effect on MnSOD activity and gene expression in mouse peritoneal macrophages. The results showed that PSK could enhance SOD activity and increase the contents of MnSOD mRNA in mouse peritoneal macrophages. Furthermore, the induction of MnSOD by PSK could be blocked by cycloheximide and actinomycin D.

L33 ANSWER 21 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:736728 HCAPLUS
DOCUMENT NUMBER: 131:346561
TITLE: A genetically modified manganese superoxide dismutase for treating oxidative damage
INVENTOR(S): McCord, Joe M.; Gao, Bifeng; Flores, Sonia C.
PATENT ASSIGNEE(S): Webb-Waring Institute for Biomedical Research, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958547	A1	19991118	WO 1999-US9921	19990506
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6190658	B1	20010220	US 1998-75019	19980508
AU 9937885	A1	19991129	AU 1999-37885	19990506

PRIORITY APPLN. INFO.: US 1998-75019 A 19980508
WO 1999-US9921 W 19990506

AB This invention discloses a genetically **modified** manganese

superoxide dismutase nucleic acid mol. and **protein**. To provide a therapeutic supplementation of the natural protection afforded tissues by endogenous superoxide dismutases (SODs) , a genetically engineered SOD was constructed that incorporates desirable features of the mitochondrial manganese superoxide dismutase (MnSOD), together with a moiety which binds to polyanionic polysaccharides or proteoglycans on endothelial cell surfaces, such as heparin and heparan sulfate. MnSOD was thus fused to the C-terminal 26 amino acids of the extracellular superoxide dismutase. The resulting modified SOD has the following identifying characteristics: (1) it binds to extracellular surfaces; (2) it extravasates quickly, reflecting its net charge; (3) it resists renal clearance; (4) it does not interfere with the bactericidal action of phagocytes; and (5) it is able to be expressed easily and economically in a high-yield expression system. The expression vector comprises: (1) a nucleic acid sequence encoding a PsodA promoter and Shine-Dalgarno sequence of Escherichia coli MnSOD; (2) an ATG translation initiation codon; (c) a nucleic acid sequence encoding human MnSOD; (4) a nucleic acid sequence encoding the C-terminal region of human extracellular SOD; (5) a nucleic acid sequence encoding a transcription termination signal of E. coli MnSOD; and (5) a nucleic acid sequence comprising a bacterial origin of replication. Also disclosed are recombinant mols., recombinant cells, therapeutic compns. and methods of using the modified manganese superoxide dismutase to treat oxidative damage. In every model examined, including both ischemia/reperfusion and inflammatory models, the modified MnSOD provides significantly and often dramatically better protection than does native MnSOD.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 22 OF 58 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2000074427 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10608715
TITLE: Modified expression of plasma glutathione peroxidase and manganese superoxide dismutase in human renal cell **carcinoma**.
AUTHOR: Sarto C; Frutiger S; Cappellano F; Sanchez J C; Doro G; Catanzaro F; Hughes G J; Hochstrasser D F; Mocarelli P
CORPORATE SOURCE: University Department of Clinical Pathology, Desio Hospital, Desio-Milan, Italy.. sarto@desiolab.unimi.it
SOURCE: Electrophoresis, (1999 Nov) 20 (17) 3458-66. Journal code: 8204476. ISSN: 0173-0835.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000105

AB Two-dimensional polyacrylamide gel electrophoresis (2-D PAGE) is a powerful tool to separate thousands of polypeptides and to highlight the modification of protein expression in **malignant** diseases. By applying 2-D PAGE to ten normal human kidney and ten homologous renal cell **carcinoma** (RCC) tissues, we found two peptides in all ten normal tissues but not in RCCs and, conversely, two peptides were detected in all RCCs but not in normal tissues. Using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) and internal sequence analysis, the two first peptides were identified as two isoforms of plasma glutathione peroxidase (GPxP). The two other peptides

isolated in all RCCs but not in normal tissues were identified by N-terminal sequence analysis as multimeric forms of manganese superoxide dismutase (Mn-SOD). No multimeric Mn-SODs and only two monomeric forms were detected in normal tissues. GPxP and Mn-SOD are metallo-enzymes encoded on chromosome 5q32 and on chromosome 6p25, respectively. Their regions are within the locus 5q21-->qter and 6q21-6q27 on which deletions and translocations are described in some cytogenetic studies of RCC transformation. Therefore, our results might suggest a correlation between the modified expression of GPxP and Mn-**SOD** in **tumor** tissues and chromosomal **modifications**, and that the two **proteins** may be putative markers for diagnosis of RCC.

L33 ANSWER 23 OF 58 MEDLINE on STN
ACCESSION NUMBER: 1998429386 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9758419
TITLE: Increased sensitivity to peroxidizing agents is correlated with an imbalance of antioxidants in normal melanocytes from melanoma patients.
AUTHOR: Grammatico P; Maresca V; Roccella F; Roccella M; Biondo L; Catricala C; Picardo M
CORPORATE SOURCE: Medical Genetic, University La Sapienza, Rome, Italy.
SOURCE: Experimental dermatology, (1998 Aug) 7 (4) 205-12. Journal code: 9301549. ISSN: 0906-6705.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981223

AB We have previously shown an imbalance of the antioxidant system in some cultures of normal melanocytes from patients with melanoma. In order to evaluate if the alteration of the antioxidants could be the basis of an increased sensitivity to exposure to peroxidative agents, in cultured melanocytes from normal individuals (n = 11) and from patients with melanoma (n = 11), superoxide dismutase and catalase activities were evaluated by spectrophotometer, and the levels of vitamin E and of the polyunsaturated **fatty** acid of cell membranes were determined by gas chromatography mass spectrometry. In 5 out of the 11 cultures of melanocytes from melanoma patients, with respect to those from normal individuals, a significant decrease of catalase activity (Cat) associated with an increase of vitamin E (Vit E) concentration was found, whereas no significant **modification** of **superoxide dismutase** activity (**SOD**) was observed. A wide range of variability was detected in the percentage of the polyunsaturated **fatty** acids of the cell membranes and a correlation was found between the ratio SOD/Cat and the percentage of linoleic acid, indicating that the imbalance of the enzymatic antioxidants leads to a lipoperoxidative process. The electron microscopic examination of these cultures revealed many microvilli in the plasma membranes and nuclear infoldings and in the cytoplasm light vacuoles. Moreover some cells contained several dense bodies with a round shape and numerous spherical lamellae possibly representing immature melanosomes. Treatment with cumene hydroperoxide between 0.66 and 20 microM did not produce a significant modification of cell viability in melanocytes from normal individuals. On the contrary in melanocytes from melanoma patients correlated with the ratio Vit E/Cat, considered as a parameter of the antioxidant imbalance, a stimulatory effect was observed at 0.66 microM

CUH and a cytotoxic effect at 20 microM. In conclusion our results suggest that a constitutional alteration of the scavenger system could be present in normal melanocytes from melanoma patients and that this could be the basis for an increased sensitivity to pro-oxidant agents.

L33 ANSWER 24 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:337367 HCAPLUS
DOCUMENT NUMBER: 129:255
TITLE: Effect of lecithinized SOD (PC-SOD) on experimental pulmonary metastasis in mice
AUTHOR(S): Takenaga, Mitsuko; Igarashi, Rie; Mizushima, Yutaka
CORPORATE SOURCE: Second Dep. of Institute of Medical Science, St. Marianna University School of Medicine, Kawasaki, 216-8512, Japan
SOURCE: Drug Delivery System (1998), 13(2), 115-121
CODEN: DDSYEI; ISSN: 0913-5006
PUBLISHER: Nippon DDS Gakkai Jimukyoku
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB In an exptl. pulmonary metastasis model employing Meth A cells, significant and dose-dependent inhibition was observed by i.v. pre-administration of PC-SOD. Unmodified SOD (U-SOD) was also effective, but was less potent than PC-SOD. The activity of endogenous SOD remained unchanged immediately after **tumor** cell implantation. PC-SOD significantly increased the SOD activity compared with that of the control group. U-SOD also increased the activity, which was more quickly reduced. In vitro addition of PC-SOD dose-dependently suppressed cell growth of Meth A, while SOD had little effect. In addition, the combination of PC-SOD and S-nitroso-N-acetyl-D,L-pencillamine (SNAP), a nitric oxide (NO) generating agent, had additive effect. It was also found that PC-SOD prevented the reduced levels of NOx in the lung following **tumor** cell inoculation. Therefore, there might be a possibility that PC-SOD was more useful to prevent the excessive formation of superoxide anions (O2-) and peroxynitrate (ONOO-) to elicit cell damage and facilitate metastatic incidence.

L33 ANSWER 25 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:286673 SCISEARCH
THE GENUINE ARTICLE: WR444
TITLE: Prolongation of the serum half-life period of superoxide dismutase by poly(ethylene glycol) modification
AUTHOR: Nakaoka R; Tabata Y; Yamaoka T; Ikada Y (Reprint)
CORPORATE SOURCE: KYOTO UNIV, BIOMED ENGN RES CTR, SAKYO KU, 53 KAWAHARA CHO, KYOTO 60601, JAPAN (Reprint); KYOTO UNIV, BIOMED ENGN RES CTR, SAKYO KU, KYOTO 60601, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: JOURNAL OF CONTROLLED RELEASE, (2 JUN 1997) Vol. 46, No. 3, pp. 253-261.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0168-3659.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 33
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Superoxide dismutase (SOD) was chemically modified using poly(ethylene glycol) (PEG) with different molecular weights to prepare PEG-**SOD conjugates** with different extents of modification. The body

distribution of the conjugates intravenously injected to mice was investigated to assess the influence of modification on the serum half-life period of SOD. The SOD modification with PEG was effective in lowering the elimination rate of SOD from the blood circulation without any change in the distribution pattern of organs other than the kidney. The molecular weight of PEG used for modification and the modification extent have a minimum effect on the half-life of the SOD. The half-life of the **SOD** and its PEG **conjugates** have a similar dependency on the apparent molecular weight as the PEG molecules. This indicates that the half-life of **SOD** and the PEG **conjugates** are mainly determined by their molecular size.

L33 ANSWER 26 OF 58 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 1998209217 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9547996
TITLE: Enteropathy associated T cell lymphoma.
AUTHOR: Wright D H
CORPORATE SOURCE: University Department of Pathology, Southampton General Hospital.
SOURCE: Cancer surveys, (1997) 30 249-61. Ref: 49
Journal code: 8218015. ISSN: 0261-2429.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980520
Last Updated on STN: 19980520
Entered Medline: 19980514

AB Enteropathy associated T cell lymphoma (EATCL) is the most serious complication of coeliac disease. HLA genotyping shows that patients with EATCL have the coeliac disease associated DQA1*0501, DQB1*0201 phenotype. Other HLA-DR/DQ alleles that may be associated with adult onset coeliac disease appear to represent additional risk factors for lymphoma development. Increased numbers of small intestinal intraepithelial cytotoxic T cells are found in the small intestinal mucosa of patients with coeliac disease and in the enteropathic bowel of patients with EATCL. The neoplastic cells of EATCL have the immunophenotype of intraepithelial cytotoxic T cells and may exhibit epitheliotropism. Analysis of T cell receptor genes and immunohistochemistry have shown that the intestinal mucosa distant from the tumour contains clonal populations of small T cells, often of the same clone as the high grade T cell lymphoma. Most cases of chronic ulcerative enteritis are probably part of the same disease process. The ulceration seen in chronic ulcerative enteritis and in enteropathy associated T cell lymphoma may be due to the release of cytolytic enzymes by cytotoxic T cells and tumour cells. These findings suggest that EATCL arises in the setting of coeliac disease and evolves from intraepithelial lymphocytosis through low grade lymphoma to a high grade **tumour**, possibly under antigen drive from **gliadin** peptides. These peptides may be presented to the intraepithelial cytotoxic T cells directly by epithelial cells bearing the coeliac disease associated HLA-DQ alleles.

L33 ANSWER 27 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:792142 SCISEARCH
THE GENUINE ARTICLE: YB987
TITLE: Post-transcriptional elevation of mouse brain Mn-SOD

protein by mercuric chloride

AUTHOR: Kumagai Y (Reprint); Mizukado S; Nagafune J; Shinyashiki M; HommaTakeda S; Shimojo N

CORPORATE SOURCE: UNIV TSUKUBA, INST COMMUNITY MED, DEPT ENVIRONM MED, TSUKUBA, IBARAKI 305, JAPAN (Reprint); UNIV TSUKUBA, MASTERS PROGRAM ENVIRONM SCI, TSUKUBA, IBARAKI 305, JAPAN; UNIV TSUKUBA, GRAD SCH, DOCTORAL PROGRAM MED SCI, TSUKUBA, IBARAKI 305, JAPAN

COUNTRY OF AUTHOR: JAPAN

SOURCE: BRAIN RESEARCH, (19 SEP 1997) Vol. 769, No. 1, pp. 178-182

Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

ISSN: 0006-8993.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 46

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Alterations in gene expression, protein content and enzyme activity of brain Mn-SOD following mercuric chloride (HgCl2) exposure were examined in ICR male mice. Subcutaneous administration of HgCl2 (1 mg Hg/kg) resulted in a significant increase (4-fold) in the brain Mn-SOD content at 6 h after injection while the total mercury concentration was about 0.11 mu g/g of brain. The enhancement of Mn-SOD protein caused by HgCl2 was completely abolished by pretreatment with dexamethasone (3 mg/kg) 1 h prior to HgCl2 administration, suggesting involvement of inflammation in inorganic mercury-induced increase in the antioxidant enzyme. This increase in level of Mn-SOD content coincided with a substantial rise in the enzyme activity; however, Northern blot analysis revealed that the induction of protein level was not due to that of its gene expression. The results of the present study indicate that mouse brain Mn-**SOD** appears to undergo post-translational **modification** by the environmental toxic metal, and induction of the antioxidant enzyme could be of an initial response to the metal-induced oxidative stress. (C) 1997 Elsevier Science B.V.

L33 ANSWER 28 OF 58 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 1997-178752 [16] WPIDS

DOC. NO. CPI: C1997-057420

TITLE: Preparation of penta aza-cyclopentadecane and -cyclohexadecane derivs. - comprises e.g. cyclisation of di amine with tri aza-alkane-di oic acid, or tri amine with di aza-alkane-di oic acid, useful in sequestering metal ions.

DERWENT CLASS: B02

INVENTOR(S): ASTON, K W; HENKE, S L; LENNON, P J

PATENT ASSIGNEE(S): (MONS) MONSANTO CO

COUNTRY COUNT: 71

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9640658	A1	19961219	(199716)*	EN	74

RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG

W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN

Search completed by David Schreiber x22526

AU 9659283	A	19961230 (199716)	
US 5721361	A	19980224 (199815)	22
EP 830351	A1	19980325 (199816)	EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE			
JP 11507621	W	19990706 (199937)	100

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9640658	A1	WO 1996-US7553	19960530
AU 9659283	A	AU 1996-59283	19960530
US 5721361	A Cont of	US 1995-486434	19950607
		US 1996-665070	19960611
EP 830351	A1	EP 1996-916578	19960530
		WO 1996-US7553	19960530
JP 11507621	W	WO 1996-US7553	19960530
		JP 1997-500694	19960530

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9659283	A Based on	WO 9640658
EP 830351	A1 Based on	WO 9640658
JP 11507621	W Based on	WO 9640658

PRIORITY APPLN. INFO: US 1995-486434 19950607; US 1996-665070 19960611

AN 1997-178752 [16] WPIDS

AB WO 9640658 A UPAB: 19970417

Preparation of a pentaaza -cyclopentadecanedione or cyclohexadecanedione derivative

of formula (I) or (II) comprises: (a) contacting a diamine of formula (III) or (IV) with a dicarboxylic acid of formula (V), its ester or anhydride, in the presence of a suitable base (SB); provided that: (i) when (V) is an ester, (SB) is optional; (ii) when (V) is the acid or the anhydride, the reaction mixture further comprises a coupling agent. R = H, alkyl, or aryl; R1-R20 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl, cycloalkylcycloalkyl, cycloalkenylalkyl, alkylcycloalkyl, alkylcycloalkenyl, alkenylcycloalkyl, alkenylcycloalkenyl, heterocyclyl, aryl, or aralkyl; R1-R12 can also be radicals attached to the alpha -C of alpha -amino acids; or R3 or R4 and R5or R6, or R7 or R8 and R9or R10, R1+R2, R3+R4, R5+R6, R7+R8, R9+R10, R11+R12 complete Q; or Q = a 3-20C opt. saturated or partially saturated ring; R1 or R2 and R3 or R4, R5 or R6 and R7 or R8, or R9 or R10 and R11or R12 complete a 2-20C azacyclyl, provided that, when the azacyclyl is aromatic and has no substit. on the N, the H attached to the N in the macrocycle, and the R gps. attached to the same C atoms of the macrocycle are absent; or R1+R2, R3+R4, R5+R6, R7+R8, R9+R10, or R11+R12 = oxo or =S and combinations of O and S; or R19, R20 = OR23, OH, SR23, NR23R24, P(=O)(OR25)(OR26), or P(=O)(OR25)R25; or R19+R20 = oxo, =S, =NOH, =NR23, =NOR23, =NOCOR23, or =CR23R24; R13 or R14 and R15 or R16 complete Q, provided that if the diamine has 3 carbon atoms between the nitrogen atoms, Q has 4-20C; or R13 or R14 and R19 or R20, or R15 or R16 and R19 or R20 complete Q and combinations of these; R23, R24 = alkyl, aryl, or aralkyl; R25, R26 = H, alkyl, aryl, or aralkyl; A, B, C = H, alkyl, aryl, aralkyl, cycloalkyl, OR21, SOR21, SO2R21, COOR21, COR21, CONR21R22,

P(=O)R21R22, P(=O)(OR21)(OR22), P(=S)R21R22, or Si(OR21)3; provided that, when two R gps. together on a C adjacent to the N are O or S, then A, B, C = H, alkyl, aralkyl, or aryl only; R21, R22 = H, alkyl, aryl, aralkyl, or alkaryl; alkyl = 1-22C; cycloalkyl = 3-10C; aryl = phenyl or naphthyl (both opt. substd.);

USE - The pentaaza macrocycles sequestrate metal ions and are therefore useful for qualitative and quantitative assay of these. The manganese complexes are low mol.weight mimetics of superoxide dismutase (SOD), useful in SOD related disorders. These include inflammatory conditions, e.g., bowel disease, reperfusion injury, rheumatoid arthritis, osteoarthritis, atherosclerosis, hypertension, **carcinogenesis** or metastasis, psoriasis, transplant rejection, radiation induced injury, thrombosis or **fatty** embolism, platelet aggregation disorder, pancreatitis, insulin dependent diabetes, intravascular coagulation, respiratory distress syndrome, asthma, influenza, stroke, burns, and trauma. The Mn (II) complexes are also useful as MRI contrast agents.

ADVANTAGE - Disadvantages of natural, recombinant, and **modified SOD** enzymes in prior art therapy, such as their lack of oral activity, short in vivo half-lives, immunogenicity with non-human derived enzymes, and poor tissue distribution are not encountered with the cpds.

Dwg.0/0

ABEQ US 5721361 A UPAB: 19980410

Prepn. of a pentaaza -cyclopentadecanedione or cyclohexadecanedione deriv. of formula (I) or (II) comprises: (a) contacting a diamine of formula (III) or (IV) with a dicarboxylic acid of formula (V), its ester or anhydride, in the presence of a suitable base (SB); provided that: (i) when (V) is an ester, (SB) is optional; (ii) when (V) is the acid or the anhydride, the reaction mixt. further comprises a coupling agent. R = H, alkyl, or aryl; R1-R20 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl, cycloalkylcycloalkyl, cycloalkenylalkyl, alkylcycloalkyl, alkylcycloalkenyl, alkenylcycloalkyl, alkenylcycloalkenyl, heterocyclyl, aryl, or aralkyl; R1-R12 can also be radicals attached to the alpha -C of alpha -amino acids; or R3 or R4 and R5or R6, or R7 or R8 and R9or R10, R1+R2, R3+R4, R5+R6, R7+R8, R9+R10, R11+R12 complete Q; or Q = a 3-20C opt. satd. or partially satd. ring; R1 or R2 and R3 or R4, R5 or R6 and R7 or R8, or R9 or R10 and R11or R12 complete a 2-20C azacyclyl, provided that, when the azacyclyl is aromatic and has no substit. on the N, the H attached to the N in the macrocycle, and the R gps. attached to the same C atoms of the macrocycle are absent; or R1+R2, R3+R4, R5+R6, R7+R8, R9+R10, or R11+R12 = oxo or =S and combinations of O and S; or R19, R20 = OR23, OH, SR23, NR23R24, P(=O)(OR25)(OR26), or P(=O)(OR25)R25; or R19+R20 = oxo, =S, =NOH, =NR23, =NOR23, =NOCOR23, or =CR23R24; R13 or R14 and R15 or R16 complete Q, provided that if the diamine has 3 carbon atoms between the nitrogen atoms, Q has 4-20C; or R13 or R14 and R19 or R20, or R15 or R16 and R19 or R20 complete Q and combinations of these; R23, R24 = alkyl, aryl, or aralkyl; R25, R26 = H, alkyl, aryl, or aralkyl; A, B, C = H, alkyl, aryl, aralkyl, cycloalkyl, OR21, SOR21, SO2R21, COOR21, COR21, CONR21R22, P(=O)R21R22, P(=O)(OR21)(OR22), P(=S)R21R22, or Si(OR21)3; provided that, when two R gps. together on a C adjacent to the N are O or S, then A, B, C = H, alkyl, aralkyl, or aryl only; R21, R22 = H, alkyl, aryl, aralkyl, or alkaryl; alkyl = 1-22C; cycloalkyl = 3-10C; aryl = phenyl or naphthyl (both opt. substd.);

USE - The pentaaza macrocycles sequestrate metal ions and are therefore useful for qualitative and quantitative assay of these. The manganese complexes are low mol.wt. mimetics of superoxide dismutase (SOD), useful in SOD related disorders. These include inflammatory conditions, e.g., bowel disease, reperfusion injury, rheumatoid arthritis,

osteoarthritis, atherosclerosis, hypertension, **carcinogenesis** or metastasis, psoriasis, transplant rejection, radiation induced injury, thrombosis or **fatty** embolism, platelet aggregation disorder, pancreatitis, insulin dependent diabetes, intravascular coagulation, respiratory distress syndrome, asthma, influenza, stroke, burns, and trauma. The Mn (II) complexes are also useful as MRI contrast agents.

ADVANTAGE - Disadvantages of natural, recombinant, and **modified SOD** enzymes in prior art therapy, such as their lack of oral activity, short in vivo half-lives, immunogenicity with non-human derived enzymes, and poor tissue distribution are not encountered with the cpds.

L33 ANSWER 29 OF 58 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1996-251534 [25] WPIDS
DOC. NO. CPI: C1996-079574
TITLE: Use of receptor agonist for controlling levels of extracellular superoxide dismutase - for treatment or prevention of diseases involving superoxide radicals or their intermediates, also useful for identifying active cpds...
DERWENT CLASS: B04
INVENTOR(S): MARKLUND, S L; STRALIN, P
PATENT ASSIGNEE(S): (MARK-I) MARKLUND S L; (STRA-I) STRALIN P
COUNTRY COUNT: 66
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9614060	A1	19960517	(199625)*	EN	69
RW: AT BE CH DE DK ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN					
AU 9537082	A	19960531	(199639)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9614060	A1	WO 1995-IB979	19951103
AU 9537082	A	AU 1995-37082	19951103
		WO 1995-IB979	19951103

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9537082	A	Based on	WO 9614060

PRIORITY APPLN. INFO: DK 1994-1283 19941104
AN 1996-251534 [25] WPIDS
AB WO 9614060 A UPAB: 19960625
Use of a substance (I) for stimulating release of extracellular superoxide dismutase (EC-SOD) from cells, or stimulating synthesis of EC-SOD in cells is new.

USE - (I) are used to treat or prevent conditions associated with presence or formation of superoxide radicals or their toxic intermediates, e.g. altered blood pressure; inflammation or formation of atherosclerotic

lesions, proliferation of arterial intima; diabetes, bronchial diseases involving inflammation and constriction (e.g. asthma); ischaemia followed by reperfusion (e.g. infarction); a wide range of inflammatory diseases (partic. acute pancreatitis), autoimmune diseases, CNS degeneration; disseminated intravascular coagulation, **fatty** embolism; burns; adverse effects of ionising radiation; **carcinogenesis**, etc. (I) after the level of EC-SOD in blood vessels, bronchi, lung, kidney, gut, CNS, cornea, joints, middle ear, skin, uterus, heart etc. by **modifying** synthesis of endogenous EC-**SOD**.
Dwg.0/6

L33 ANSWER 30 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:382539 SCISEARCH
THE GENUINE ARTICLE: UK390
TITLE: EVALUATION OF SOME ANTIOXIDANT ENZYMES IN LUNG-**CARCINOMA** TISSUE
AUTHOR: GUNER G; ISLEKEL H (Reprint); OTO O; HAZAN E; ACIKEL U
CORPORATE SOURCE: DEPT THORAC & CARDIOVASC SURG, INCIRALTI 35340, IZMIR, TURKEY (Reprint); DEPT THORAC & CARDIOVASC SURG, INCIRALTI 35340, IZMIR, TURKEY; DOKUZ EYLUL UNIV, FAC MED, DEPT BIOCHEM, INCIRALTI 35340, IZMIR, TURKEY
COUNTRY OF AUTHOR: TURKEY
SOURCE: CANCER LETTERS, (05 JUN 1996) Vol. 103, No. 2, pp. 233-239

ISSN: 0304-3835.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB This investigation was effected to determine the levels of the two antioxidant enzymes, superoxide dismutase (SOD) (EC 1.15.1.1) and catalase (CAT) (EC 1.11.1.6) in lung **cancerous** tissues and to compare with normal lung tissue in order to evaluate the antioxidant status in lung **cancer**. Fifteen lung **carcinoma** tissue samples and the normal counterparts from the same cases were homogenized and the cytosols obtained by ultracentrifugation (100 000 x g). **SOD** was assayed using a **modification** of the indirect nitroblue tetrazolium assay method, while CAT was measured by a spectrophotometric method. The data obtained are as follows: 1.42 +/- 0.24 U/mg protein (means +/- SEM) of SOD in lung **cancer** and 3.13 +/- 0.51 U/mg protein in normal lung tissue and 33.53 +/- 6.09 U/mg protein of CAT in lung **cancer** and 71.33 +/- 14.38 in normal lung tissue. The differences were found to be significant at the level of $P < 0.01$ for both enzymes. These low levels of the antioxidant enzymes in lung **cancerous** tissues can lead to elevated levels of reactive oxygen metabolites, resulting in damage to the key subcellular structures such as DNA, cell membranes, and other vital cellular components.

L33 ANSWER 31 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:540345 SCISEARCH
THE GENUINE ARTICLE: UX134
TITLE: BIOLOGICAL EFFECTS OF DIESEL EXHAUST PARTICLES (DEP) .3. PATHOGENESIS OF ASTHMA LIKE SYMPTOMS IN MICE
AUTHOR: SAGAI M (Reprint); FURUYAMA A; ICHINOSE T
CORPORATE SOURCE: NATL INST ENVIRONM STUDIES, RES TEAM HLTH EFFECTS AIR POLLUTANTS, TSUKUBA, IBARAKI 305, JAPAN (Reprint); NATL INST ENVIRONM STUDIES, DIV ENVIRONM HLTH STUDIES, IBARAKI, OSAKA 305, JAPAN

COUNTRY OF AUTHOR: JAPAN
SOURCE: FREE RADICAL BIOLOGY AND MEDICINE, (1996) Vol. 21, No. 2, pp. 199-209.
ISSN: 0891-5849.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 82

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Chronic airway inflammation, mucus hypersecretion, reversible airway constriction, and bronchial hyperresponsiveness are important pathogenic features of asthma. We found that diesel exhaust particles (DEP) instilled intratracheally and repeatedly to mice (once/week for 16 weeks) caused marked infiltration of inflammatory cells, proliferation of goblet cells, increased mucus secretion, respiratory resistance, and airway constriction. Eosinophils in the submucosa of the proximal bronchi and medium bronchioles increased eightfold following instillation. Eosinophil infiltration was significantly suppressed by pretreatment with polyethyleneglycol-**conjugated superoxide dismutase** (PEG-**SOD**). Bound sialic acid concentrations in bronchial alveolar lavage fluids, an index of mucus secretion, increased with DEP, but were suppressed by pretreatment with PEG-SOD. Goblet cell hyperplasia, airway narrowing, and airway constriction also were observed with DEP. Respiratory resistance in the DEP-group to acetylcholine was 11 times higher than in controls, and the increased resistance was significantly suppressed by PEG-SOD pretreatment. These findings suggest that DEP and/or oxygen radicals derived from DEP cause bronchial asthma in mice.

L33 ANSWER 32 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:551530 SCISEARCH
THE GENUINE ARTICLE: UX857
TITLE: INFLUENCE OF PERCUSSION TRAUMA ON EXPRESSION OF INTERCELLULAR-ADHESION MOLECULE-1 (ICAM-1) BY HUMAN CEREBRAL MICROVASCULAR ENDOTHELIUM
AUTHOR: GOURIN C G; SHACKFORD S R (Reprint)
CORPORATE SOURCE: UNIV VERMONT, COLL MED, DEPT SURG, FLETCHER 301, FAHC, 111 COLCHESTER AVE, BURLINGTON, VT, 05401 (Reprint); UNIV VERMONT, COLL MED, DEPT SURG, BURLINGTON, VT, 05401
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF TRAUMA-INJURY INFECTION AND CRITICAL CARE, (JUL 1996) Vol. 41, No. 1, pp. 129-135.
ISSN: 1079-6061.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 41

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Objectives: Brain injury is associated with the production of oxygen free radicals (OFR) and the accumulation of polymorphonuclear leukocytes (PMN) at the site of injury, both of which may be involved in the evolution of secondary cerebral injury, Intercellular adhesion molecule-1 (ICAM-1) is responsible for adherence of PMNs. We sought to determine whether percussion trauma altered the expression of ICAM-1 and to determine the effect of OFR scavengers on ICAM-1 expression after percussion trauma.

Design: Prospective controlled laboratory research using passage 2 human cerebral microvascular endothelium (HCME).

Materials and Methods: Cell lysates were collected over 24 hours and

analyzed for ICAM-1 by enzyme-linked immunosorbent assay (ELISA) after trauma or incubation with **tumor** necrosis factor (TNF)-alpha. OFR scavengers were added immediately after trauma with or without previous incubation with TNF-alpha.

Measurements and Main Results: Sublethal percussion trauma did not alter ICAM-1 expression by HCME. TNF-alpha upregulated ICAM-1 in percussed and nonpercussed cells with maximal ICAM-1 expression at 24 hours ($p < 0.01$, ANOVA), However, percussion trauma significantly blunted the response of HCME to TNF-alpha. The addition of OFR scavengers after percussion trauma alone had no effect on ICAM-1 expression at 24 hours, but restored the response of percussed HCME to TNF-alpha.

Conclusions: Percussion trauma alters the response of HCME to cytokine-induced ICAM-1 upregulation, and the normal response is restored by OFR scavengers, This suggests that HCME become dysfunctional after percussion trauma and this dysfunction may be mediated by OFR.

L33 ANSWER 33 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1995:851893 HCAPLUS
DOCUMENT NUMBER: 123:251741
TITLE: An antioxidant extract of Cucumis melo high in catalase and superoxide dismutase for use in cosmetics, pharmaceuticals, or foods
INVENTOR(S): Ginoux, Jean-Paul; Dreyer, Alain; Roch, Philippe; Baccou, Jean-Claude; Lacan, Dominique
PATENT ASSIGNEE(S): Bio-Obtention SC, Fr.
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 670366	A1	19950906	EP 1995-400449	19950302
EP 670366	B1	20010606		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2716884	A1	19950908	FR 1994-2459	19940303
FR 2716884	B1	19961004		
ES 2158054	T3	20010901	ES 1995-400449	19950302
JP 08048699	A2	19960220	JP 1995-68874	19950303
JP 3467748	B2	20031117		
US 5616323	A	19970401	US 1995-398940	19950303
US 5747043	A	19980505	US 1996-775802	19961231

PRIORITY APPLN. INFO.: FR 1994-2459 A 19940303
US 1995-398940 A1 19950303

AB An extract of Cucumis melo that is high in superoxide dismutase (>30 units/mg protein) and catalase (>45 units/mg protein) and that is useful as an antioxidant is described for use in pharmaceuticals, cosmetics and foods.

L33 ANSWER 34 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:210863 SCISEARCH
THE GENUINE ARTICLE: TY998
TITLE: EFFECTS OF GRANULOCYTE-COLONY-STIMULATING FACTOR UPON COXSACKIEVIRUS B3 MYOCARDITIS IN MICE
AUTHOR: HIRAOKA Y; KISHIMOTO C (Reprint); TAKADA H; SUZAKI N; SHIRAKI K
CORPORATE SOURCE: TOYAMA MED & PHARMACEUT UNIV, FAC MED, DEPT INTERNAL MED 2, 2630 SUGITANI, TOYAMA 93001, JAPAN (Reprint); TOYAMA

MED & PHARMACEUT UNIV, FAC MED, DEPT INTERNAL MED 2, TOYAMA 93001, JAPAN; TOYAMA MED & PHARMACEUT UNIV, FAC MED, DEPT VIROL, TOYAMA 93001, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: EUROPEAN HEART JOURNAL, (DEC 1995) Vol. 16, No. 12, pp. 1900-1906.
ISSN: 0195-668X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 25
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Granulocyte colony-stimulating factor is a potent activator of mature granulocytes, and subsequently enhances superoxide release. The purpose of this study was to investigate the effects of granulocyte colony-stimulating factor upon marine coxsackievirus B3 myocarditis in relation to free radical-mediated cardiac damage. Two-week-old, male, C3H/He mice were inoculated intraperitoneally with coxsackievirus B3. Granulocyte colony-stimulating factor 20 mu g.kg(-1).day(-1), polyethylene glycol-**conjugated superoxide dismutase** (an enzyme catalyzing the conversion of O-2(-) to H2O2) 1 x 10(3) U.kg(-1).day(-1) and granulocyte colony-stimulating factor 20 mu g.kg(-1).day(-1), plus polyethylene glycol-**conjugated superoxide dismutase** 1 x 10(3) U.kg(-1).day(-1), were injected subcutaneously daily on days 0 to 14. Treated groups were compared to the infected, untreated group. The survival rate in the polyethylene glycol-**conjugated superoxide dismutase** group was higher than that of the untreated group on day 14, but on day 7, cardiac pathology was not significantly different among the four groups. On day 14, the scores of cellular infiltration, myocardial necrosis and calcification were lower in the polyethylene glycol-**conjugated superoxide dismutase** group and in the granulocyte colony-stimulating factor plus polyethylene glycol-**conjugated superoxide dismutase** group than in the untreated group. The myocardial virus titres on days 7 and 14 dis not differ significantly among the four groups. The number of total white blood cell and neutrophil counts were significantly greater in the granulocyte colony-stimulating factor group than in the untreated group on day 7. Taken altogether with the previous reports and present evidence that the administration of granulocyte colony-stimulating factor did not exacerbate coxsackievirus B3 myocarditis, it may be that oxygen-free radicals appeared to be derived not from leukocytes but from other components in this experimental model of myocarditis, whereas the myocardium was inflamed with leukocytes.

L33 ANSWER 35 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 95:298241 SCISEARCH
THE GENUINE ARTICLE: QU832
TITLE: EFFECT OF TYPE OF DIETARY-FAT AND ETHANOL ON ANTIOXIDANT ENZYME MESSENGER-RNA INDUCTION IN RAT-LIVER
AUTHOR: NANJI A A (Reprint); GRINIUVIENE B; SADRZADEH S M H; LEVITSKY S; MCCULLY J D
CORPORATE SOURCE: NEW ENGLAND DEACONESS HOSP, DEPT PATHOL, BOSTON, MA, 02215 (Reprint); HARVARD UNIV, SCH MED, BOSTON, MA, 02215; NEW ENGLAND DEACONESS HOSP, DIV CARDIOTHORAC SURG, BOSTON, MA, 02215
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF LIPID RESEARCH, (APR 1995) Vol. 36, No. 4, pp. 736-744.

ISSN: 0022-2275.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 61

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We carried out a study to relate the effect of the type of dietary fat and ethanol on antioxidant enzyme mRNA levels in liver in the intragastric feeding rat model. Different types of dietary fat were administered [saturated fat (SE), corn oil (CE) and fish oil (FE)] with ethanol to induce varying severities of liver injury. Ethanol-fed rats were pair-fed with dextrose-fed controls that received isocaloric amounts of dextrose. All animals were killed at 1 month and the following studies were carried out: evaluation of severity of pathologic liver injury, mRNA quantitation for catalase, glutathione peroxidase (GPx), and manganese **superoxide dismutase** (MnSOD), microsomal **conjugated** dienes, and hydrogen peroxide. SE animals had no liver injury, FE animals had severe liver injury, and CE animals had moderate liver injury. Ethanol induced GPx mRNA in all dietary groups, with the highest levels seen in the FE group. The pattern of catalase mRNA induction was similar to that of GPx mRNA. In contrast, MnSOD mRNA was decreased compared to controls in animals that developed pathologic liver injury, i.e., CE and FE groups. A positive correlation was seen between conjugated diene levels and GPx mRNA ($r = 0.88$, $P < 0.01$) and catalase mRNA. The similar slopes for the relationship between conjugated dienes and catalase in the fish oil and non-fish oil groups indicate that the same degree of lipid peroxidation increases catalase mRNA to a greater degree in fish oil-fed rats. A positive correlation was also seen between catalase mRNA and H2O2 ($r = 0.95$, $P < 0.001$). We propose that the increase in catalase and GPx mRNA levels is probably in response to enhanced lipid peroxidation; the decrease in MnSOD mRNA may predispose the cells to liver injury.

L33 ANSWER 36 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:432973 HCAPLUS
DOCUMENT NUMBER: 121:32973

TITLE: Functional consequences of the binding of gliadin to cultured rat mesangial cells: bridging immunoglobulin A to cells and modulation of eicosanoid synthesis and altered cytokine production

AUTHOR(S): Amore, Alessandro; Emancipator, Steven N.; Roccatello, Dario; Gianoglio, Bruno; Peruzzi, Licia; Porcellini, Maria Gabriella; Piccoli, Giuseppe; Coppo, Rosanna
CORPORATE SOURCE: Nephrol. Dial. Dep., Regina Margherita Hosp., Turin, 10126, Italy

SOURCE: American Journal of Kidney Diseases (1994), 23(2), 290-301
CODEN: AJKDDP; ISSN: 0272-6386
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oral immunization with gliadin (GLI) can induce IgA mesangial deposits (IgA nephropathy [IgAN]) in mice. A role for GLI in human IgAN has been inferred from an association with celiac disease, increased serum anti-GLI IgA in patients with IgAN, and benefit from a gluten-free diet observed in some IgAN patients. These effects might be due to the antigenic or lectinic properties of GLI. The aim of the authors' study was to investigate whether GLI binding to glycosylated residues (ie, lectinic activity) favors binding of GLI to cultured rat mesangial cells, bridging IgA macromols. The authors also sought to determine whether GLI binding alters

mesangial cell function. Gliadin binds to rat mesangial cells in the third and fourth passages, as determined by immunofluorescence. Gliadin binding is inhibited by co-incubation with 1 mol/L N-acetyl-D-glucosamine and 1 mol/L α-D-mannose, sugars competitive for this lectinic bond. Quantification by biotinylated GLI revealed a significant dose-dependent binding of GLI inhibited by N-acetyl-D-glucosamine. Some saccharolytic enzymes, like invertase, modify the cell surface to decrease GLI binding. In addition, GLI promoted the binding of purified mouse polymeric IgA to mesangial cells. The binding of GLI to mesangial cells modulates arachidonic acid metabolism by cultured mesangial cells, significantly inhibiting prostaglandin E2 production, increasing synthesis of thromboxane B2 and tumor necrosis factor, but not interleukin-1β. These responses were abrogated by co-incubation with N-acetyl-D-glucosamine and/or pretreatment with invertase. Non-immune binding of an environmental alimentary lectin, GLI, to mesangial cells in culture might favor the binding of IgA and IgAIC to mesangial cells, enhancing both IgA mesangial trapping and in situ IgA deposit formation. This could occur via GLI-specific antibodies or by virtue of the binding of nonspecific IgA on a lectinic basis, or both. Related changes in eicosanoid synthesis might stimulate mesangial cell growth and mesangial matrix production, together with mesangial cell contraction, contributing to the pathogenesis of IgAN.

L33 ANSWER 37 OF 58 MEDLINE on STN
ACCESSION NUMBER: 93246435 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8482686
TITLE: Polyethylene glycol-**conjugated superoxide dismutase** protects rats against oxygen toxicity.
AUTHOR: Tang G; White J E; Gordon R J; Lumb P D; Tsan M F
CORPORATE SOURCE: Research Service, Samuel S. Stratton Department of Veterans Affairs Medical Center, Albany, New York.
SOURCE: Journal of applied physiology (Bethesda, Md. : 1985), (1993 Mar) 74 (3) 1425-31.
Journal code: 8502536. ISSN: 8750-7587.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 19930618
Last Updated on STN: 19930618
Entered Medline: 19930601

AB Superoxide dismutase (SOD) has an important role in the protection against O2 toxicity. **Conjugation** of Cu,Zn-**SOD** to polyethylene glycol (PEG-SOD) prolongs its plasma half-life and facilitates its cellular uptake. However, prior studies have shown that intravenous injection of PEG-SOD does not protect animals against O2 toxicity. In this study, we demonstrated that tracheal insufflation of PEG-SOD resulted in a dose-dependent protection against O2 toxicity. Nine of 15 rats (60%) insufflated with 25,000 U PEG-SOD survived continuous 100% O2 exposure for more than 7 days compared with control rats (n = 45), all of which died within 3 days of O2 exposure ($P < 0.025$). In contrast, insufflation of 25,000 U SOD, 9.7 mg methoxy-PEG (equivalent to the amount of methoxy-PEG present in 25,000 U PEG-SOD), or a combination of SOD and methoxy-PEG had no protective effect. Furthermore, intravenous or intraperitoneal injection of PEG-SOD did not afford significant protection. Protection against O2 toxicity by PEG-SOD insufflation was associated with attenuated O2-induced pulmonary injury as evidenced by a reduced volume of pleural effusion. Insufflation of PEG-SOD markedly increased pulmonary SOD activity (to 300 and 370% of controls at 24 and 50 h, respectively)

without affecting pulmonary catalase activity. We conclude that insufflation of PEG-SOD protects rats against O2 toxicity, possibly by enhancing pulmonary SOD activity.

L33 ANSWER 38 OF 58 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 94203402 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8152564
TITLE: [Gastroenterologic pathology and replacement organotherapy in thyroidectomized patients].
Patologia gastroenterica e opoterapia sostitutiva nei pazienti tiroidectomizzati.
AUTHOR: Certo M; Mancini A; Fiumara C; Conte G; Valle D; Abagnale R; Rabitti C; De Marinis L
CORPORATE SOURCE: Istituti di Clinica Medica Generale, Universita Cattolica del Sacro Cuore, Roma.
SOURCE: Minerva chirurgica, (1993 Nov) 48 (21-22) 1319-23.
Journal code: 0400726. ISSN: 0026-4733.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940523
Last Updated on STN: 19940523
Entered Medline: 19940512

AB Thyroid replacement therapy in patients treated by near-total or total thyroidectomy, as well as spontaneous hypothyroidism , can be difficult in patients with alterations in absorption functions or specific gastroenteric diseases. We have studied 25 patients, 22 women and 3 men, 18-72 years old (mean 47 years), affected by spontaneous or post-surgical hypothyroidism, who presented, during the usual replacement therapy, persistently elevated or high-normal TSH levels, and therefore required repeated variations in the prescribed dose of thyroxine. In these patients we evaluated hormone pattern, the presence of autoantibodies (anti-tyroglobulin, anti-Sm, anti-DNA, anti-microsomal antigens, anti-**gliadin** and anti-parietal cell), and performed an esophagogastroduodenoscopy (EGD) with histological examination. In all patients, plasma TSH ranged from 2.5 to 20 microU/ml. Only 17% of patients exhibited the presence of antibodies against thyroglobulin, 17% of patients had antibodies against microsomal antigens, 6% of patients presented antibodies against nuclear antigens; 4% had against **gliadin**. Histological examination revealed chronic gastritis (98%) with atrophic aspects (20%) and intestinal metaplasia (28%); and chronic duodenitis (86%) with villus abnormalities (23%) and total villus atrophy (4%). We underline the case of a patient, **treated** by total thyroidectomy for papillary **carcinoma**, who presented, two months after starting L-thyroxine therapy, a recurrence of celiac disease, that had been silent after childhood. The EGD showed, at the level of the second duodenal segment, a reduction of number and thickness of mucosal folds; the histological examination showed total villus atrophy, elongated crypts and a dense infiltration of chronic inflammatory cells in the lamina propria. Our experience underlines the frequent association of gastroenteric disease and hypothyroidism.(ABSTRACT TRUNCATED AT 250 WORDS)

L33 ANSWER 39 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 93:733665 SCISEARCH
THE GENUINE ARTICLE: MK939
TITLE: **CONJUGATION** OF CU,ZN-**SUPEROXIDE** **DISMUTASE** WITH SUCCINYLATED GELATIN -

Search completed by David Schreiber x22526

PHARMACOLOGICAL ACTIVITY AND CELL-LUBRICATING FUNCTION
AUTHOR: KOJIMA Y; HARUTA A; IMAI T; OTAGIRI M; MAEDA H (Reprint)
CORPORATE SOURCE: KUMAMOTO UNIV, DEPT MICROBIOL, HONJO 2-2-1, KUMAMOTO 860, JAPAN; KUMAMOTO UNIV, FAC PHARMACEUT SCI, KUMAMOTO 860, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: BIOCONJUGATE CHEMISTRY, (NOV/DEC 1993) Vol. 4, No. 6, pp. 490-498.
ISSN: 1043-1802.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 52

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Superoxide dismutase (SOD) and succinylated gelatin (succinyl gelatin) were conjugated to improve in vivo pharmacological activity of SOD. Lysyl residues of human recombinant Cu,Zn-SOD were cross-linked with carboxyl residues of succinyl gelatin using 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide. Various chemical and pharmacokinetic parameters of the conjugate were determined. Analysis by atomic absorption spectrometry and amino acid composition revealed that the conjugate was composed of about 2.9 mol of succinyl gelatin (with a mean molecular weight of 23 000) to 1 mol of SOD and exhibited an apparent mean molecular weight of 98 000. The conjugate retained almost 100% of its original activity on a molar basis. When the succinyl gelatin-**conjugated** Cu,Zn-**SOD** (Suc-gel-SOD) was administered intravenously to mice, its plasma half-life was prolonged to 29.7 min compared with 4.5 min for native SOD. Tissue distribution analysis revealed that intravenously administered Suc-gel-SOD showed a much greater accumulation than native SOD in the liver followed by in decreasing order the kidney, the lung, and the spleen; native SOD was excreted more rapidly into urine before it accumulated in tissues. Furthermore, Suc-gel-SOD exhibited lower antigenicity and immunogenicity than native SOD, and it had a better therapeutic effect against ischemic edema of the foot pad in mice. The conjugate was found to accumulate more than native SOD in the ischemic foot pad. A newly added property of the conjugate is cell-lubricating activity, which facilitated cell passage through micropores and reduced hemolysis during cell passage in vitro. Thus, Suc-gel-SOD appears to be a promising protein drug with greatly improved pharmacological properties in vivo while possessing the same enzyme activity as native SOD.

L33 ANSWER 40 OF 58 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 94039517 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8223958
TITLE: Involvement of free radicals in cisplatin-induced emesis in Suncus murinus.
AUTHOR: Torii Y; Mutoh M; Saito H; Matsuki N
CORPORATE SOURCE: Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, University of Tokyo, Japan.
SOURCE: European journal of pharmacology, (1993 Aug 2) 248 (2) 131-5.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19970203

Search completed by David Schreiber x22526

Entered Medline: 19931221

AB The participation of free radicals in cisplatin-induced emesis was investigated in the house musk shrew, Suncus murinus. Thiobarbituric acid (TBA) values, which indicate the degree of lipid peroxidation, in brain, liver and small intestine were increased significantly 60 min after the treatment with cisplatin (20 mg/kg, i.p.). Moreover, cisplatin (20 mg/kg, i.p.)-induced emesis was prevented by intraperitoneal injection of N-(2-mercaptopropionyl)glycine (MPG), a radical scavenging agent, with ID50 value of 130 mg/kg. However, MPG did not block the emesis induced by copper sulfate (40 mg/kg, p.o.), veratrine (0.5 mg/kg, s.c.) or serotonin (10 mg/kg, i.p.). We also investigated the effects of **superoxide dismutase conjugated** to polyethylene glycol and catalase, but the number of vomiting episodes and latency did not change significantly when these agents were intraperitoneally injected 30 min prior to or 20 min after the administration of cisplatin. MPG did not affect the antitumor effect of cisplatin tested in vitro. These results suggest that free radicals mediate emesis caused by cisplatin and that radical scavengers may become a new class of prophylactic drug against **cancer**-chemotherapeutic drug-induced emesis.

L33 ANSWER 41 OF 58 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1994:274232 BIOSIS
DOCUMENT NUMBER: PREV199497287232
TITLE: Involvement of free radicals in cisplatin-induced emesis in Suncus murinus.
AUTHOR(S): Torii, Yoshifumi; Mutoh, Masato; Saito, Hiroshi; Matsuki, Norio [Reprint author]
CORPORATE SOURCE: Dep. Chem. Pharmacol., Fac. Pharm. Sci., Univ. Tokyo 7-3-1 Hongo, Bunkyo, Tokyo 113, Japan
SOURCE: European Journal of Pharmacology Environmental Toxicology and Pharmacology Section, (1993) Vol. 2, No. 2, pp. 131-135.
ISSN: 0926-6917.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jun 1994
Last Updated on STN: 25 Jun 1994

AB The participation of free radicals in cisplatin-induced emesis was investigated in the house musk shrew, Suncus murinus. Thiobarbituric acid (TBA) values, which indicate the degree of lipid peroxidation, in brain, liver and small intestine were increased significantly 60 min after the treatment with cisplatin (20 mg/kg, i.p.). Moreover, cisplatin (20 mg/kg, i.p.)-induced emesis was prevented by intraperitoneal injection of N-(2-mercaptopropionyl)glycine (MPG), a radical scavenging agent, with ID-50 value of 130 mg/kg. However, MPG did not block the emesis induced by copper sulfate (40 mg/kg, p.o.), veratrine (0.5 mg/kg, s.c.) or serotonin (10 mg/kg, i.p.). We also investigated the effects of **superoxide dismutase conjugated** to polyethylene glycol and catalase, but the number of vomiting episodes and latency did not change significantly when these agents were intraperitoneally injected 30 min prior to or 20 min after the administration of cisplatin. MPG did not affect the antitumor effect of cisplatin tested in vitro. These results suggest that free radicals mediate emesis caused by cisplatin and that radical scavengers may become a new class of prophylactic drug against **cancer**-chemotherapeutic drug-induced emesis.

L33 ANSWER 42 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 93:526710 SCISEARCH

Search completed by David Schreiber x22526

THE GENUINE ARTICLE: LU126
TITLE: INVOLVEMENT OF FREE-RADICALS IN CISPLATIN-INDUCED EMESIS IN SUNCUS-MURINUS
AUTHOR: TORII Y; MUTOH M; SAITO H; MATSUKI N (Reprint)
CORPORATE SOURCE: UNIV TOKYO, FAC PHARMACEUT SCI, DEPT CHEM PHARMACOL, 7-3-1 HONGO, BUNKYO KU, TOKYO 113, JAPAN; TORAY INDUSTRIES LTD, BASIC RES LABS, KANAGAWA 248, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY-ENVIRONMENTAL TOXICOLOGY AND PHARMACOLOGY SECTION, (02 AUG 1993) Vol. 248, No. 2, pp. 131-135.
ISSN: 0926-6917.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 32
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The participation of free radicals in cisplatin-induced emesis was investigated in the house musk shrew, Suncus murinus. Thiobarbituric acid (TBA) values, which indicate the degree of lipid peroxidation, in brain, liver and small intestine were increased significantly 60 min after the treatment with cisplatin (20 mg/kg, i.p.). Moreover, cisplatin (20 mg/kg, i.p.)-induced emesis was prevented by intraperitoneal injection of N-(2-mercaptopropionyl)glycine (MPG), a radical scavenging agent, with ID50 value of 130 mg/kg. However, MPG did not block the emesis induced by copper sulfate (40 mg/kg, p.o.), veratrine (0.5 mg/kg, s.c.) or serotonin (10 mg/kg, i.p.). We also investigated the effects of **superoxide dismutase conjugated** to polyethylene glycol and catalase, but the number of vomiting episodes and latency did not change significantly when these agents were intraperitoneally injected 30 min prior to or 20 min after the administration of cisplatin. MPG did not affect the antitumor effect of cisplatin tested in vitro. These results suggest that free radicals mediate emesis caused by cisplatin and that radical scavengers may become a new class of prophylactic drug against **cancer**-chemotherapeutic drug-induced emesis.

L33 ANSWER 43 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:162702 HCAPLUS
DOCUMENT NUMBER: 118:162702
TITLE: Biological effects of diesel exhaust particles. I. In vitro production of superoxide and in vivo toxicity in mouse
AUTHOR(S): Sagai, Masaru; Saito, Hiroki; Ichinose, Takamichi; Kodama, Masahiko; Mori, Yoki
CORPORATE SOURCE: Natl. Inst. Environ. Stud., Tsukuba, 305, Japan
SOURCE: Free Radical Biology & Medicine (1993), 14(1), 37-47
CODEN: FRBMEH; ISSN: 0891-5849
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The problem of whether or not active oxygen species are involved in pulmonary injury by diesel exhaust particles (DEP) was investigated. It was found that DEP could produce superoxide O2•- and hydroxyl radical (•OH) in vitro without any biol. activating systems. In this reaction system, O2•- prodns. were inhibited by the addition of superoxide dismutase (SOD) and DMSO, resp. DEP which were washed with methanol could no longer produce O2•- and •OH, indicating that active components were extractable with organic solvents. These oxygen radicals were also identified by ESR measurement. DEP instilled intratracheally to mouse caused high mortality at low dose, although methanol-washed DEP did not

kill any mouse. The cause of death seemed to be pulmonary edema mediated by endothelial cell damage. The instilled DEP markedly decreased the activities of SOD, glutathione peroxidase, and glutathione S-transferase in mouse lungs. The death rate and lung injury were markedly prevented by polyethylene glycol-**conjugated SOD** (PEG-**SOD**) pretreatment prior to DEP administration. The mortality and lung injury by DEP were also suppressed by BHT pretreatment. From these results, it was suggested that most parts of DEP toxicity in lungs are due to active oxygen radicals such as O2•- and •OH, and that the cause of death is due to pulmonary edema mediated by endothelial cell damage.

L33 ANSWER 44 OF 58 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 94354937 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8074791
TITLE: Protective effect of nickel chloride on superoxide damage: enhancement of CuZn superoxide dismutase affinity to the oxygen free radical.
AUTHOR: Novelli E L; Rodrigues N L; Ribas B O
CORPORATE SOURCE: Department of Chemistry, Universidade Estadual Paulista, UNESP, Sao Paulo, Brazil.
SOURCE: Boletin de estudios medicos y biologicos, (1993 Jan-Dec) 41 (1-4) 28-32.
Journal code: 0136501. ISSN: 0067-9666.
PUB. COUNTRY: Mexico
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941013
Last Updated on STN: 19970203
Entered Medline: 19941004

AB The effect of nickel from soluble NiCl2 on Cu-Zn superoxide dismutase (SOD) activity, as well as on rate of nitro blue tetrazolium reduction, was studied in vitro since **lipid** peroxidation has been implicated in cell damage by nickel insoluble compounds, whose toxicity and **carcinogenicity** are well established. The physical and chemical nature of nickel compounds is one of the key determinations of its toxicity. Soluble nickel freely enter cells, but is just as readily excreted reducing the opportunity for production of **lipid** damage. Nickel from NiCl2 strongly activated SOD activity. In vitro addition of nickel chloride to a crude lung preparation altered the KM for SOD without changing the Vmax. Nickel chloride produced increased enzyme affinity to the substrate, because decreased (O2-) concentration that yields half-maximal velocity. The combination of nickel and **SOD** may contribute to **stabilization** of the particular conformation of **SOD** responsible for maximal catalytically activity.

L33 ANSWER 45 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 92:230772 SCISEARCH
THE GENUINE ARTICLE: HM442
TITLE: DNA-BASE MODIFICATIONS INDUCED IN ISOLATED HUMAN CHROMATIN BY NADH DEHYDROGENASE-CATALYZED REDUCTION OF DOXORUBICIN
AUTHOR: AKMAN S A (Reprint); DOROSHOW J H; BURKE T G; DIZDAROGLU M
CORPORATE SOURCE: CITY HOPE NATL MED CTR, DEPT MED ONCOL & THERAPEUT RES, 1500 E DUARTE RD, DUARTE, CA, 91010 (Reprint); NATL INST STAND & TECHNOL, CHEM SCI & TECHNOL LAB, GAITHERSBURG, MD, 20899
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMISTRY, (07 APR 1992) Vol. 31, No. 13, pp. 3500-3506

Search completed by David Schreiber x22526

ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 46

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The antineoplastic benzanthroquinone drug doxorubicin can undergo flavoenzyme-catalyzed one-electron reduction which, in an aerobic environment, leads to the generation of oxygen-derived species. We therefore sought to determine whether doxorubicin in the presence of NADH dehydrogenase and the transition metal ions Fe(III) or Cu(II) induces DNA base modifications in isolated human chromatin. NADH dehydrogenase-catalyzed reduction of doxorubicin (25-100-mu-M) caused hydroxyl radical production detected as methane generated from dimethyl sulfoxide; addition of isolated human chromatin to the system produced a concentration-dependent quenching of detectable hydroxyl radical formation. Doxorubicin (5-50-mu-M)-stimulated enzyme-catalyzed oxidation of NADH was also diminished, but still detectable, in the presence of chromatin. Doxorubicin-induced DNA base modifications in chromatin were measured by gas chromatography/mass spectrometry with selected-ion monitoring. Production of modified bases required the addition of transition metal ion and was enhanced by the addition of active flavoenzyme. The non-redox cycling analogue 5-iminodaunorubicin induced significantly less base modification than did doxorubicin. In the presence of Fe(III), NADH dehydrogenase-catalyzed reduction of doxorubicin caused enhancement in the content of all modified bases over control levels. Substitution of Cu(II) for Fe(III) altered both the degree and the pattern of doxorubicin/NADH dehydrogenase-induced base modifications. The scavengers of hydroxyl radical mannitol and dimethyl sulfoxide or catalase did not significantly affect doxorubicin/NADH/NADH dehydrogenase/transition metal ion-induced base **modifications. Superoxide dismutase**
further enhanced production of all base modifications. The data demonstrate that flavoenzyme-catalyzed redox cycling of doxorubicin generates typical hydroxyl radical-induced base modifications in the DNA of isolated human chromatin, suggesting a possible mechanism for the mutagenicity of doxorubicin in vivo.

L33 ANSWER 46 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 92:700862 SCISEARCH
THE GENUINE ARTICLE: KA151
TITLE: ANTIOXIDANTS ATTENUATE MICROVASCULAR CHANGES IN THE EARLY PHASE OF EXPERIMENTAL PNEUMOCOCCAL MENINGITIS IN RATS
AUTHOR: PFISTER H W (Reprint); KOEDEL U; LORENZL S; TOMASZ A
CORPORATE SOURCE: UNIV MUNICH, KLINIKUM GROSSHADERN, DEPT NEUROL, MARCHIONINISTR 15, W-8000 MUNICH 70, GERMANY (Reprint); ROCKEFELLER UNIV, NEW YORK, NY, 10021
COUNTRY OF AUTHOR: GERMANY; USA
SOURCE: STROKE, (DEC 1992) Vol. 23, No. 12, pp. 1798-1804.
ISSN: 0039-2499.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 39

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background and Purpose: We tested in a rat meningitis model 1) whether pneumococcal cell wall components are capable of producing changes in regional cerebral blood flow, brain water content, and intracranial pressure similar to those we have already observed after intracisternal

inoculation of live pneumococci and 2) whether antioxidants would modulate these alterations in the early phase of meningitis.

Methods: Regional cerebral blood flow as measured by laser Doppler flowmetry and intracranial pressure were monitored continuously for 4 hours after intracisternal challenge. Brain edema formation was assessed by brain water content determinations. We investigated the following groups: rats challenged intracisternally with the whole intact pneumococcal cell wall (n=7) or the pneumococcal cell wall hydrolyzed by the M1-muramidase (n=7); rats injected intracisternally with phosphate-buffered saline (n=6); rats pretreated intravenously with **superoxide dismutase conjugated** with polyethylene glycol (10,000 units/kg) and injected intracisternally with cell wall components (n=5) or phosphate-buffered saline (n=6); rats injected intracisternally with phosphate-buffered saline and pretreated intravenously with polyethylene glycol (10% solution, 1.2 ml/kg, n=5) or continuously treated with intravenous free superoxide dismutase (22,000 units/kg per hour, n=6); and rats continuously treated intravenously with deferoxamine mesylate (10 mg/kg per hour) and injected intracisternally with cell wall components (n=6) or phosphate-buffered saline (n=7).

Results: Both pneumococcal cell wall preparations produced a significant increase in regional cerebral blood flow, intracranial pressure, and brain water content. **Conjugated superoxide dismutase** as well as deferoxamine prevented the increase in intracranial pressure and brain water content. In addition, the increase in regional cerebral blood flow as observed in untreated, cell wall-challenged rats (baseline, 100%; 183.1+/-12.3% after 4 hours, mean+/-SEM) was significantly attenuated by administration of both **conjugated superoxide dismutase** (136.6+/-14.1%) and deferoxamine (149.8+/-8.2%) ($p<0.05$). Polyethylene glycol-**conjugated superoxide dismutase** alone produced an increase in regional cerebral blood flow (125.6+/-8.7% after 4 hours). We found that polyethylene glycol per se accounts for this action.

Conclusions: These data show that pneumococcal cell wall components containing teichoic acid produce changes in regional cerebral blood flow, intracranial pressure, and brain water content and that oxygen radicals contribute to these pathophysiological alterations in the early phase of experimental pneumococcal meningitis.

L33 ANSWER 47 OF 58 EMBASE on STN

ACCESSION NUMBER:	92321753 EMBASE
DOCUMENT NUMBER:	1992321753
TITLE:	Polyoxyethylene-**modified superoxide dismutase** reduces side effects of adriamycin and mitomycin C.
AUTHOR:	Kawasaki S.; Akiyama S.; Kurokawa T.; Kataoka M.; Dohmitsu K.; Kondoh K.; Yamauchi M.; Ito K.; Watanabe T.; Sugiyama S.; Ozawa T.; Matsuyama M.; Takagi H.
CORPORATE SOURCE:	Department of Surgery II, Nagoya University School of Medicine, 65 Tsurumai-cho,Showa-ku, Nagoya 466, Japan
SOURCE:	Japanese Journal of Cancer Research, (1992) 83/8 (899-906). ISSN: 0910-5050 CODEN: JJCREP
COUNTRY:	Japan
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	016 Cancer 029 Clinical Biochemistry 030 Pharmacology 037 Drug Literature Index 038 Adverse Reactions Titles

LANGUAGE: English
SUMMARY LANGUAGE: English
AB Polyoxyethylene-**modified superoxide dismutase** (**SOD**-POE) is a newly developed long-acting superoxide dismutase. Adriamycin (ADR) and mitomycin C (MMC) generate superoxide, which contributes to their cytocidal effects or side effects. We examined whether SOD-POE could prevent the side effects induced by superoxide generated by antitumor agents, and the following results were obtained. SOD-POE did not influence the antitumor effects of ADR and MMC either in vitro or in vivo, but prevented the toxic death of BALB/c, nu/nu male mice caused by overdoses of ADR or MMC. As for its effective sites, SOD-POE prevented a decrease in the specific activity of rotenone-sensitive NADH-ubiquinone oxido-reductase (complex I) in heart muscle mitochondrial respiratory chain function in BALB/c male mice administered 10 mg/kg ADR, and prevented damage to the sarcoplasmic reticulum and mitochondria of mouse heart muscle by ADR as observed by electron microscopy. Furthermore, SOD-POE prevented bone marrow suppression induced by MMC in Donryu rats. The above results suggest that combination chemotherapy with SOD-POE would make it possible to increase the maximum permissible doses of antitumor agents, improving the efficacy of these agents.

L33 ANSWER 48 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 1991:422201 HCAPLUS
DOCUMENT NUMBER: 115:22201
TITLE: **Superoxide dismutase**-catalase **conjugates** as tissue-specific therapeutics
INVENTOR(S): Poznansky, Mark J.; Mao, Guo Dong
PATENT ASSIGNEE(S): University of Alberta, Can.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9103548	A1	19910321	WO 1990-CA279	19900830
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
CA 2065430	AA	19910301	CA 1990-2065430	19900830
AU 9062854	A1	19910408	AU 1990-62854	19900830
US 5336493	A	19940809	US 1992-836274	19920302
PRIORITY APPLN. INFO.:			GB 1989-19661	19890831
			WO 1990-CA279	19900830

AB A novel multicomponent **conjugate** having **superoxide dismutase** (**SOD**), catalase, and optionally albumin and a targeting agent such as antibody is provided. A pharmaceutical composition containing such conjugate can be used for tissue-specific scavenging of superoxide and hydroxyl radicals with higher efficiency than SOD or catalase alone. The half-life of the **SOD**-catalase **conjugates** was 300 min in rats. Scavenging of the free radicals using the conjugates was also demonstrated in vitro and in the rat heart model of ischemia-reperfusion.

L33 ANSWER 49 OF 58 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1991-009803 [02] WPIDS
DOC. NO. CPI: C1991-004325
TITLE: Modified biologically active protein - e.g.

superoxidedismutase, for improved of disease, e.g. diabetes and kidney **cancer**.

DERWENT CLASS: B04 D16

INVENTOR(S): MIZUSHIMA, Y

PATENT ASSIGNEE(S): (ASAG) ASAHI GLASS CO LTD; (LTTK-N) LTT KENKYUSHO KK; (MIZU-I) MIZUSHIMA Y; (SEGK) SEIKAGAKU CORP; (SEGK) SEIKAGAKU KOGYO CO LTD

COUNTRY COUNT: 18

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 406804	A	19910109	(199102)*		13
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
AU 9058652	A	19910110	(199109)		
CA 2020439	A	19910107	(199113)		
JP 03163100	A	19910715	(199134)		
JP 03170438	A	19910724	(199136)		
US 5109118	A	19920428	(199220)		8
EP 406804	A3	19920401	(199328)		13
AU 647027	B	19940317	(199416)		
US 5310958	A	19940510	(199418)		7
US 5362491	A	19941108	(199444)		8
EP 406804	B1	19960117	(199608)	EN	15
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
DE 69024862	E	19960229	(199614)		
ES 2084621	T3	19960516	(199627)		
JP 2679852	B2	19971119	(199751)		4
JP 2718809	B2	19980225	(199813)		7
CA 2020439	C	19981124	(199906)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 406804	A		EP 1990-112690	19900703
JP 03163100	A		JP 1990-176297	19900705
JP 03170438	A		JP 1989-310056	19891129
US 5109118	A		US 1990-547039	19900702
EP 406804	A3		EP 1990-112690	19900703
AU 647027	B		AU 1990-58652	19900704
US 5310958	A	Div ex	US 1990-547039	19900702
			US 1992-832585	19920207
US 5362491	A	Div ex	US 1990-547039	19900702
		Div ex	US 1992-832585	19920207
			US 1994-190451	19940202
EP 406804	B1		EP 1990-112690	19900703
DE 69024862	E		DE 1990-624862	19900703
			EP 1990-112690	19900703
ES 2084621	T3		EP 1990-112690	19900703
JP 2679852	B2		JP 1989-310056	19891129
JP 2718809	B2		JP 1990-176297	19900705
CA 2020439	C		CA 1990-2020439	19900704

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 647027	B	Previous Publ.	AU 9058652

Search completed by David Schreiber x22526

US 5362491	A	Div ex	US 5109118
.		Div ex	US 5310958
DE 69024862	E	Based on	EP 406804
ES 2084621	T3	Based on	EP 406804
JP 2679852	B2	Previous Publ.	JP 03170438
JP 2718809	B2	Previous Publ.	JP 03163100

PRIORITY APPLN. INFO: JP 1989-174371 19890706; JP 1989-310056 19891129

AN 1991-009803 [02] WPIDS

AB EP 406804 A UPAB: 19940303

A modified biologically active protein (A) comprises a protein bonded to **lecithin** via a chemical linkage. The constituent protein is pref. an antibody or superoxide dismutase. Pref. (A) is of the formula: A(X-B)k, where A is a protein residue, B is a lysolecithin residue with a hydroxyl gp. at the 2-position of glycerol which lacks a hydrogen bond, and X is the chemical linkage and K is at least 1 bond.

USE/ADVANTAGE - (A) is used, in oral or local admin., in association with a protease inhibitor which does not inhibitor it for treating diseases such as diabetes (in which case the protein constituent would be insulin), multiple myeloma or osteoporosis. Production of (A) is easy compared to conventional rpods. and the modification is possible irrespective of the solubility of the protein. **Lecithin** is non-toxic and therefore safe.

In an example, the hair was removed from the back of a C3H mouse and an electric iron heated to 400 deg C was used to burn it. **Lecithin -modified SOD** was i.v. administered prior to the burning and 30 mins. after the burning. Healing was shown to be significantly quicker in the gp. treated with the **lecithin-modified SOD** compared to a non-treated control gp.

@(13pp Dwg.No.0/0)

0/0

ABEQ US 5109118 A UPAB: 19930928

A new modified biologically active protein is of formula A(X-B)k, where A is residue of biologically active protein, B is residue of lysolecithin bonded to X by OH gp. at 2-position of glycerol; X is covalent linking gp; k is integer 1 to NO. functional gps. of the biologically active protein. Pref. X is -C(O)R10(O)- or -C(O)R2C(O)NHR1C(O)- where R1 and R2 are each alkylene. Biologically active proteins include antiibodies, superoxidedismutase, insulin, and kallidinogenase.

USE/ADVANTAGE - Compsns. of biologically active proteins bonded to **lecithin** give more effective drug delivery systems than drugs encapsulated in liposome or **lipid** microspheres, both as regards longterm maintainance of drug concn. in body and reduction of side effects, and allows oral admin. of many drugs which previously had to be injected.

ABEQ US 5310958 A UPAB: 19940622

Lecithin deriv. is of formula Z-R3-C(O)-B (I) where B is a lysolecithin residue having OH at the glycerol 2-position with the H of the OH removed; R3 is -R2-C(O)NH-R1 or a S-contg. gp.; R1-2 are each 1-24C alkylene; and Z is carboxyl, protected carboxyl or carbonyl bonded to an active ester.

USE/ADVANTAGE - In a drug delivery system to administer biologically active proteins, antibodies, SOD, insulin and kallidinogenase. Selective migration to site. Improved pharmacological effects. Reduced side-effects.

Dwg.0/0

ABEQ US 5362491 A UPAB: 19941223

Protein compsn. comprises a biologically active protein, e.g. an antibody, superoxide dismutase, insulin or callidinogenase, that has been modified

by covalent linkage to **lecithin** and a protease inhibitor which does not interfere with the biological activity.

USE/ADVANTAGE - The prods. are orally or locally administered therapeutics. The prods. exhibit improved assimilation, cell specificity and biological action without unwanted side effects.

Dwg.0/0

ABEQ EP 406804 B UPAB: 19960227

The modified biologically active protein which is represented by the formula A(X-B)k (I), wherein A is a residue of the biologically active protein, B is a residue of lysolecithin having a hydroxyl group at the 2-position of glycerol, with the hydrogen atom of said hydroxyl group removed, X is the chemical linkage, and k is a bond number of at least 1.

Dwg.0/0

L33 ANSWER 50 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:137413 HCAPLUS

DOCUMENT NUMBER: 114:137413

TITLE: Cloning of gene for human fibronectin analogs, its recombinant manufacture, and pharmaceuticals containing same

INVENTOR(S): Vogel, Tikva; Levanon, Avigdor; Werber, Moshe; Guy, Rachel; Panet, Amos

PATENT ASSIGNEE(S): Bio-Technology General Corp., USA

SOURCE: PCT Int. Appl., 295 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9007577	A1	19900712	WO 1989-US5875	19891229
W: AU, DK, FI, JP, KR, NL				
RW: AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, SE				
CA 2006929	AA	19900629	CA 1989-2006929	19891229
AU 9049598	A1	19900801	AU 1990-49598	19891229
AU 636596	B2	19930506		
EP 451211	A1	19911016	EP 1990-902086	19891229
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04505698	T2	19921008	JP 1990-502804	19891229
JP 3095771	B2	20001010		
DK 9101280	A	19910829	DK 1991-1280	19910628
US 5455158	A	19951003	US 1993-58241	19930504
US 5679320	A	19971021	US 1994-259569	19940614
US 5965383	A	19991012	US 1995-409750	19950324
US 5869616	A	19990209	US 1997-826885	19970408
US 6121426	A	20000919	US 1997-909140	19970811

PRIORITY APPLN. INFO.:

US 1988-291951	A	19881229
US 1989-345952	A	19890428
CA 1989-2006929	A	19891229
WO 1989-US5875	A	19891229
US 1990-526397	A3	19900521
US 1991-703842	B1	19910521
US 1993-58241	A1	19930504
US 1994-259569	A3	19940614
US 1995-409750	A3	19950324

AB Fibronectin fragments containing the cell-binding domain or the fibrin-binding domain for use inter alia as platelet-aggregation inhibitors, in wound

healing and in the prevention of iatrogenic infections are manufactured by expression of a cDNA encoding the domain in Escherichia coli. These fragments are not necessarily the same as those derived by proteolysis of fibronectin. A fibronectin cDNA was cloned from a human liver cDNA bank in λgt11 using oligonucleotides probes for regions of the N-terminal and cell-binding domains. After recovery of the complete sequence the regions encoding individual domains were subcloned and expressed in E. coli. In platelet aggregation inhibition assays a 40 kilodalton cell-binding domain inhibited aggregation 40% at 0.5 μM. In the same assay the pentapeptide GRGDS was as effective at 25 μM. The 31 kilodalton fibrin-binding domain was shown to bind to Staphylococcus aureus as effectively as the comparable proteolytic fragment.

L33 ANSWER 51 OF 58 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 91077806 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2175248
TITLE: Immunotargeting approach utilizing production of oxygen free radicals.
AUTHOR: Mashiba H; Matsunaga K
CORPORATE SOURCE: Division of Immunology, 3-1-1 Notame, Fukuoka, Japan.
SOURCE: Cancer letters, (1990 Dec 17) 55 (3) 183-8.
Journal code: 7600053. ISSN: 0304-3835.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910322
Last Updated on STN: 19970203
Entered Medline: 19910129

AB **Tumor**-specific inhibition of cell proliferation through production of oxygen free radicals was studied by using immunoconjugates. Diethyldithiocarbamate (DDC), an inhibitor of **superoxide dismutase** activity (**SOD**), was **conjugated** with anti-Meth A **tumor** cell antibodies. The addition of these conjugates in combination with ascorbic acid (AsA) induced marked inhibition of Meth A **tumor** cell proliferation. Pretreatment of the target cells with these conjugates followed by the addition of AsA was also effective in inhibiting cell proliferation. However, the pretreatment of the target cells with unconjugated anti-Meth A **tumor** cell antibodies in combination with AsA eliminated the DDC conjugate-mediated antiproliferative effect. These results suggest that the combined use of DDC-anti Meth A **tumor** cell antibody conjugates with AsA may be a beneficial approach to **cancer** therapy.

L33 ANSWER 52 OF 58 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 91:29150 SCISEARCH
THE GENUINE ARTICLE: EQ689
TITLE: IMMUNOTARGETING APPROACH UTILIZING PRODUCTION OF OXYGEN FREE-RADICALS
AUTHOR: MASHIBA H (Reprint); MATSUNAGA K
CORPORATE SOURCE: DIV IMMUNOL, 3-1-1 NOTAME, MINAMI KU, FUKUOKA 815, JAPAN (Reprint)
COUNTRY OF AUTHOR: JAPAN
SOURCE: CANCER LETTERS, (1990) Vol. 55, No. 3, pp. 183-188.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH

Search completed by David Schreiber x22526

REFERENCE COUNT: 16

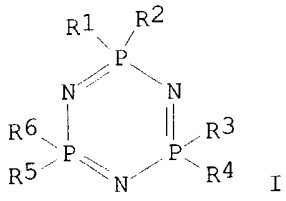
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Tumor**-specific inhibition of cell proliferation through production of oxygen free radicals was studied by using immunoconjugates. Diethyldithiocarbamate (DDC), an inhibitor of **superoxide dismutase** activity (**SOD**), was **conjugated** with anti-Meth A **tumor** cell antibodies. The addition of these conjugates in combination with ascorbic acid (ASA) induced marked inhibition of Meth-A **tumor** cell proliferation. Pretreatment of the target cells with these conjugates followed by the addition of AsA was also effective in inhibiting cell proliferation. However, the pretreatment of the target cells with unconjugated anti-Meth A **tumor** cell antibodies in combination with AsA eliminated the DDC conjugate-mediated antiproliferative effect. These results suggest that the combined use of DDC-anti Meth A **tumor** cell antibody conjugates with AsA may be a beneficial approach to **cancer** therapy.

L33 ANSWER 53 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:21146 HCAPLUS
DOCUMENT NUMBER: 112:21146
TITLE: Preparation of cyclotriphosphazene derivatives bound to hydrophilic polymer and therapeutic physiologically active substance
INVENTOR(S): Suzuki, Yoshiki; Nawata, Kyoshi; Makino, Juji
PATENT ASSIGNEE(S): Teijin Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01175999	A2	19890712	JP 1987-330218	19871228
JP 07051592	B4	19950605		

PRIORITY APPLN. INFO.: JP 1987-330218 19871228
GI



I

AB Cyclotriphosphazene derivs. [I; ≥1 of R1-R6 = hydrophilic polymer or its derivative such as polyethylene glycol, monomethoxypolyethylene glycol, polypropylene glycol, copolymer of ethylene oxide and propylene oxide, dextran, insulin, pullulan, chondroitin, etc.; ≥1 of the other R1-R6 = therapeutic physiol. active substance or its derivative containing 1 or ≥2 groups selected from OH, NH2, NH, or SH such as peptide hormones (insulin, calcitonin, and natriuretic peptide), enzymes (superoxide dismutase, asparaginase, and bilirubin oxidase), proteins (Hb, TPA, and

interferon), anticancer agents (mitomycin C, daunorubicin, and doxorubicin), and steroids (estradiol 3-Me ether, testosterone, and triamcinolone acetonide); when the number of the above substituents is ≤5, the rest of R1-R6 = 1 or ≥2 of OR7, NHR8, NR9R10, C1-24 alkyl, or halo; OR7 = tyrosine residue, C1-24 alkoxy; NHR8 = amino acid residue or C1-24 alkylamino; R9, R10 = C1-24 alkyl] which impart the therapeutic physiol. active substance such advantages as the increased bioavailability, prolonged half-life, reduced side-effect such as antigenicity, enhanced delivery to diseased sites, and high safety margin, are prepared Thus, treatment of monomethoxypolyethylene glycol (II) with NaH in THF to give the Na alcoholate followed by reaction with hexachlorocyclotriphosphazene in THF gave II-cyclotriphosphazene which was reacted with glycine Et ester (III) to give, after purification by gel filtration, II, III-cyclotriphosphazene (IV) containing 1 Cl for each cyclotriphosphazene ring. The latter compound (1.5 g) and 15 mg superoxide dismutase (V) were allowed to react 2 h at 4° in 5 mL 0.1M phosphate buffer (pH 9.0) and diluted with 0.1M phosphate buffer (pH 7.0) to give, after removal of unreacted IV by ultrafiltration and purification by gel filtration, 15 mg II, III-cyclotriphosphazene-V containing 1 II, 1 V, and 4 III. This V derivative retained .apprx.70% of V activity, showed the serum half-life of 15.2 h vs. that of 1.6 h for V, did not produce antibody due to passive anaphylaxis reaction in mice, and increased the absorption through duodenum in rats. Also prepared were II, III-cyclotriphosphazene bound to insulin, asparaginase, mitomycin C, doxorubicin, daunomycin, and estradiol 3-Me ether.

L33 ANSWER 54 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:16188 HCAPLUS
DOCUMENT NUMBER: 106:16188
TITLE: **Superoxide dismutase** depletion induces **lipid modification** in rat liver microsomal membranes
AUTHOR(S): Bartoli, Gianna Maria; Giannattasio, Bartolo; Palozza, Paola; Cittadini, Achille
CORPORATE SOURCE: Inst. Gen. Pathol., Cathol. Univ., Rome, Italy
SOURCE: Superoxide Superoxide Dismutase Chem., Biol. Med., Proc. Int. Conf., 4th (1986), Meeting Date 1985, 435-7. Editor(s): Rotilio, Giuseppe. Elsevier: Amsterdam, Neth.
CODEN: 55GJAL
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Rat liver superoxide dismutase (SOD) measured in 1- and 7-day-old newborns was 27.7% and 31.3%, resp., of that of normal adults. Adult rats made deficient in Cu had 15.8% SOD of normal. Liver microsomal membranes from Cu-deficient rats produced 30% less malondialdehyde than controls; also polyunsatd. **fatty** acids were decreased and monoenoic and saturated **fatty** acids were increased. In contrast neonatal liver membranes had slightly increased polyunsatd. **fatty** acids. Evidently, **SOD** depletion **modifies** cell membranes. The alterations observed in Cu deficiency but not in newborns resemble those observed in **tumor** cells.

L33 ANSWER 55 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:83287 HCAPLUS
DOCUMENT NUMBER: 104:83287
TITLE: Cytotoxic effects of wheat gliadin-derived peptides
AUTHOR(S): Paganuzzi, A. Stammati; Zucco, F.; Cardelli, M.; De Angelis, I.; Mattei, R.; Pino, A.; Rocca, E.;

Zampaglioni, F.
CORPORATE SOURCE: Lab. Tossicol. Comp. Ecotossicol., Ist. Super. Sanita, Rome, 00161, Italy
SOURCE: Toxicology (1985), 37(3-4), 225-32
CODEN: TXCYAC; ISSN: 0300-483X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The peptic-tryptic-Cotazym (PTC) digest, obtained from bread wheat gliadin by simulating in vivo protein digestion, was more active than the PTC-digest of durum wheat gliadin in reversibly inhibiting HEp-2 cell proliferation and in increasing cellular acid phosphatase [9001-77-8]. Colony-forming ability of the cells was not affected by treatment with either bread or durum wheat gliadin peptides. The peptic-tryptic digest of bread wheat gliadin also showed agglutinating activity with HEp-2 cells.

L33 ANSWER 56 OF 58 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:292212 BIOSIS
DOCUMENT NUMBER: PREV198478028692; BA78:28692
TITLE: OXIDATION OF AMMONIA AND HYDROXYLAMINE TO NITRATE IN THE RAT AND IN-VITRO.
AUTHOR(S): SAUL R L [Reprint author]; ARCHER M C
CORPORATE SOURCE: DEP MED BIOPHYS, UNIV TORONTO, ONT CANCER INST, TORONTO M4X 1K9, CAN
SOURCE: Carcinogenesis (Oxford), (1984) Vol. 5, No. 1, pp. 77-82.
CODEN: CRNGDP. ISSN: 0143-3334.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Ammonia is oxidized to nitrate in the rat. Male Sprague-Dawley rats gavaged with 1000 μmol 15N-ammonium chloride each day for 5 days excreted low, but significant amounts of excess 15N-nitrate in their urines on the 5 days of treatment and on the 5 subsequent days. A total of 0.28 ± 0.03 μmol excess 15N-nitrate (mean ± SE) was recovered per rat, which indicates that ammonia is converted to nitrate in a yield of .apprx. 0.0080%. The oxidation of 15N-labeled glycine and L-glutamic acid to 15N-nitrate could not be detected. 15N-Hydroxylamine was oxidized in the rat to 15N-nitrate in a yield of 4.7%, which shows that hydroxylamine is a possible intermediate in the ammonia oxidation process. Injection of rats with Arochlor 1254, an inducer of several isozymes of cytochrome P-450, did not significantly affect the rate of endogenous nitrate synthesis. Carbon tetrachloride, which causes hepatic **lipid** peroxidation, produced a small but significant increase in nitrate synthesis. A bacterial endotoxin can greatly stimulate nitrate synthesis. Concurrent treatment with **superoxide dismutase** does not **modify** the effect of the endotoxin.
An in vitro chemical model system was used to demonstrate that oxidation of ammonia to nitrate by the hydroxyl radical at physiological pH is chemically feasible. Ammonia is oxidized to nitrate in vivo by a non-enzymatic process which involves active oxygen species such as the hydroxyl radical. Apparently, a 215 g rat produces 3.0 μmol of nitrate per day via ammonia oxidation. [The existence of such an oxidation process in man may be important since nitrate and nitrite formed in this way could act as precursors of **carcinogenic** N-nitroso compounds.].

L33 ANSWER 57 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1937:1172 HCAPLUS
DOCUMENT NUMBER: 31:1172
ORIGINAL REFERENCE NO.: 31:155i,156a

Search completed by David Schreiber x22526

TITLE: Lysine and malignant growth. II. Effect on **malignant** growth of a **gliadin** diet
AUTHOR(S): Voegtlin, Carl; Maver, Mary E.
SOURCE: Public Health Reports (1936), 51, 1436-44
CODEN: PHRPA6; ISSN: 0033-3549
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Normal growth of young mice and the growth of a spontaneous mammary carcinoma of adult mice are inhibited by a diet containing gliadin as the source of protein. The addition of lysine renders this diet adequate for both normal and malignant growth. Similar expts. with a diet in which glutenin takes the place of **gliadin** indicate that normal and **malignant** growth are not inhibited. Since gliadin is known to be deficient in the indispensable normal growth-factor lysine, whereas glutenin is a complete protein, it is concluded that lysine is an essential factor necessary for the growth of the mammary carcinoma. Eight references.

L33 ANSWER 58 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1937:1171 HCAPLUS
DOCUMENT NUMBER: 31:1171
ORIGINAL REFERENCE NO.: 31:155g-i
TITLE: Lysine and malignant growth. I. The amino acid lysine as a factor controlling the growth rate of a typical neoplasm
AUTHOR(S): Voegtlin, Carl; Thompson, J. W.
SOURCE: Public Health Reports (1936), 51, 1429-36
CODEN: PHRPA6; ISSN: 0033-3549
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB A diet composed essentially of 70% ground wheat and 30% whole milk powder promotes normal growth in young rats and rapid growth of spontaneous mammary carcinoma in mice. If the milk powder of this diet has been subjected to heat under the specified conditions, the resulting diet is inadequate for normal growth, and malignant growth, as a rule, is greatly inhibited. This inhibition of normal and **malignant** growth is removed by the **administration** of lysine. An adequate supply of lysine in utilizable form is therefore necessary for the rapid growth of the malignant tumor used in these expts. Ten references.